CIBMTR® CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH

Summary and Recommendations of the 2012 Center-Specific Outcomes Analysis Forum Held on September 14, 2012

Background

In 1986, the National Bone Marrow Donor Registry (managed by the National Marrow Donor Program (NMDP)) was established, with responsibility for the maintenance of an unrelated donor registry for hematopoietic cell transplantation (HCT). In 1990, the Transplants Amendment Act made the reporting of center-specific outcomes for unrelated donor HCT mandatory in the United States. This activity has been conducted by the NMDP since 1994. With the Stem Cell Therapeutic and Research Act of 2005, the requirement to report outcomes of HCT by transplant center was broadened to include all allogeneic (related and unrelated) HCTs in the United States. This responsibility rests with the contractor for the Stem Cell Therapeutic Outcomes Database, the Center for International Blood and Marrow Transplant Research (CIBMTR).

The CIBMTR has collaborated closely with the NMDP since 2003 in the generation of center outcomes reports for unrelated donor HCT for the Health Resources and Services Administration (HRSA), a division of the U.S. Department of Health and Human Services. These reports are well-accepted by the HCT community. However, the Stem Cell Act of 2005 substantially expanded the patient population to be considered in these analyses. At most centers, the new requirement means that the percentage of patients included at least doubled. Centers that do not perform unrelated donor HCTs were included in these analyses for the first time.

During the transition phase of the C.W. Bill Young Cell Transplantation Program (the Program), CIBMTR, working with the NMDP, the American Society for Blood and Marrow Transplantation (ASBMT) and HRSA, held a meeting to review the current approach to center-specific outcomes reporting and to provide recommendations for future reports in the expanded Program. With this purpose, CIBMTR invited representatives of the HCT community (national and international), the ASBMT Committee on Quality Outcomes, governmental funding agencies, the solid organ transplant community, patients, private payers, statisticians and experts in hospital and quality outcomes reporting to Milwaukee, Wisconsin in September of 2008.

The objectives of the meeting were to review the current state of center-specific outcomes reporting in medicine and transplantation and to openly discuss strengths and limitations of current approaches with the goal of developing recommendations for HCT center outcomes reports that would be:

- scientifically valid;
- equitable;
- free from bias;
- useful to the HCT community for improving quality;
- informative for the public.

One of the recommendations of the 2008 meeting was to hold regular reviews of the process. The second Center-Specific Outcomes Analysis Forum was held on September 10, 2010. Presentations covered topics regarding current center outcomes methodology in HCT, risk factors known to affect HCT outcomes, risk adjustment in outcomes reporting, best outcomes to analyze, outcomes for investigational HCT, and presentation of outcomes to the lay community.

The third Center-Specific Outcomes Analysis Forum was held on September 14, 2012. Attendees are listed in Attachment A. Presentations covered topics regarding benefits and challenges of the HCT co-morbidity index (HCT-CI); alternative methods to attribute disease risk; suggested changes to the data collection forms for the Program; information that can made available to centers, in addition to the center outcomes report, for performance improvement; and presentation of outcomes to transplant centers, payers and the public. What follows is a summary of the discussion and recommendations from this meeting, organized by general topic.

GENERAL DISCUSSION

The current process, analytic techniques and results of the center-specific analysis were reviewed, together with changes that have been incorporated since the 2010 Center Outcomes Forum.

Since 2010, changes to the published outcomes report include:

- Full inclusion of both related and unrelated donor transplants performed in the United States.
- Implementation of a three-year rolling time window to replace the previous five-year time frame.
- Requirement of a minimum of 90% follow-up of survivors at one year for inclusion of the center in the analysis.
- Modification of the risk-adjustment model to include:
    - Full set of HCT-CI data available;
    - Finer resolution of upper age categories;
    - Breakdown of nonmalignant disease types.
- Provision of more information in the report to center directors.

There was general consensus that the current methods and analytic techniques were robust and no new recommendations were provided.

HCT CO-MORBIDITY INDEX (HCT-CI)

Collection of the HCT-CI[1] was instituted in late 2007 based upon recommendations of the ASBMT Committee on Quality Outcomes. These data are collected routinely for all HCT recipients reported to the CIBMTR on the pre-transplant essential data (pre-TED) form. HCT-CI scores are systematically available for all allogeneic recipients since 2008. CIBMTR first tested the performance of the HCT-CI in 2011 using transplants reported in 2008 and 2009. For the 2012 report, HCT CI data was collected for recipients in all three included years (2008-2010).

The HCT-CI is a composite weighted score derived from organ function assessment and presence of important comorbidities at time of transplant. Higher scores have generally been associated with higher transplant-related mortality and shorter overall survival, though some small studies have not reproduced the initial findings reported by Sorror et al[2-10]. The CIBMTR has always included an adjustment for reported comorbidities in the multivariate analysis for one-year survival, though previous assessments have used simple ratings of comorbidity by organ system. Although use of the HCT-CI may lead to better adjustment for comorbidities, additional effort is required to collect and report the data. CIBMTR is committed to testing the HCT-CI in the center-specific survival regression model to determine whether it has a significant effect on expected one-year survival rates for individual transplant centers. If the HCT-CI will continue to be used in the center-specific analysis, accurate reporting across centers is crucial. Several studies have raised questions about the validity and reliability of the index, related to institutional performances, sample size, and variability in score assignment.

Validation studies using the HCT-CI

Dr. Sorror presented information on the development and validation of the HCT-CI. The original index was developed using recipients of myeloablative and non-myeloablative HCT using related and unrelated donors in adults and children with malignant and non-malignant hematologic disorders. Scores for comorbidities were assigned based upon their hazard ratios for effect on non-relapse mortality.

Since its publication in 2005, a substantial number of investigators have tried to reproduce the findings. Many have been able to reproduce the effect of the HCT-CI on outcomes in the original categories defined by Sorror; others have not. The studies which have not confirmed the findings of Sorror have been limited by sample size, reliability of defining the comorbidities, or substantial differences in the incidence of comorbidities.

Results of a multi-center validation study from the Seattle Consortium were reported. In this study a single evaluator reviewed the scoring of the comorbidities. Substantial variation occurred in missing values for comorbidities between the centers. The HCT-CI score predicted overall survival and non-relapse mortality well in this study.

Although the comorbidity index has good predictive value for overall survival and non-relapse mortality when consistently evaluated by a trained observer (validity), it was acknowledged that the inter-rater reliability should be improved. Ideas presented to improve the inter-rater reliability include development of consistent methods of data acquisition, better coding guidelines, and better training of data professionals. Use of enhanced training and coding guidelines at a single center led to high inter-rater reliability (weighted Kappa of 0.9) using previously inexperienced evaluators.

Preliminary data regarding the potential predictive value of pre-transplant ferritin, albumin and platelet count on non-relapse mortality were presented.

Inter-rater reliability of HCT-CI at HCT centers

CIBMTR also completed a study comparing the inter-rater reliability between the comorbidity index (HCT-CI) originally reported by the data professional to that derived from a retrospective physician review of the medical record of the patients at four participating centers. Two different processes, leading to different score reliability, were evident at these centers. In some cases, the data professional reviews the chart and completes the form using available data, whereas in others the physician caring for the patient assigns and documents the HCT-CI. In a randomly selected cohort of patients from these four centers, the inter-rater reliability, as measured by the kappa statistic, ranged from 0.28 to 0.80, suggesting substantial variability between the original assessment and the retrospective assessment at some centers. Results were similar when each comorbid factor was assessed or when evaluating by the cumulative score for each patient. The retrospective score assigned by a physician was often higher than the originally reported score. Inconsistent results could affect a center's rating.

Review of the data reported for the HCT-CI by the CIBMTR demonstrates there is high utilization of the "other comorbidity" field in the comorbidity section. In fact, the "other comorbidity" field was completed in approximately 30% of patients included in the validation study. Commonly reported other comorbidities include hypertension, gastroesophageal reflux disease, hyperlipidemia, hypothyroidism, osteoporosis, and deep vein thrombosis. In some cases, centers report a comorbidity under the "other specify" section that should clearly have been reported as a designated category (e.g., prior breast cancer reported as an "other specify" rather than the category of "prior solid tumor"). Approximately 5% of the items reported in the "other specify" field have sufficient information to be coded as a specifically defined comorbidity. This suggests there is a lack of understanding of reporting comorbidities at some centers. Insufficiently reported data may lead to under-reporting of comorbidities.

Operationalizing the HCT-CI at a center

A single center's approach to collecting and reporting the HCT-CI was presented. Reporting the HCT-CI creates a number of challenges for centers, including the broad spectrum of co-morbidities covered, the scope of general medical knowledge required, and its labor-intensive nature. This center developed a model in which the transplant physician can quickly complete a draft HCT-CI, using a tool in the EMR, based on the

pre-HCT evaluation. The HCT-CI is finalized after the conditioning regimen is initiated so that all assessments pre-transplant can be included. A data professional completes this step, verifying the information entered by the clinician against the medical record. Questionable data is adjudicated by the clinician. Even using this system, some errors in coding the comorbidities are frequently encountered. These include: over-attribution of obesity through lack of formal confirmation of BMI, under-reporting of psychiatric illness, double coding of mild and moderate organ dysfunction, and ambiguity regarding which previous malignancies to report as "prior solid tumors."

General Discussion:

There was general consensus that the HCT-CI has discriminative predictive value for one-year survival and should continue to be collected and used to adjust for comorbidity in the center-specific analysis. However, several of the limitations to its reliability and validity were discussed. There was general concern that inter-rater reliability is quite variable at some centers where agreement between raters is only moderate. There is ambiguity in the definition of some comorbidities, and others are subject to judgment of the rater.

Several suggestions for future research were discussed. Will the HCT-CI remain valid once the reliability is increased? Might there be differences in the outcome prediction between centers with known reliable assessment compared to other centers? Does training of data professionals at centers improve reliability and affect predictive value of the HCT? Further research is needed to determine whether serum ferritin, albumin and platelet counts assessed pre-HCT add predictive value to the comorbidity index.

Although the "other specify" field within the comorbidity reporting section of the forms may lead to spurious reporting, it was also acknowledged that occasional review of this field may be valuable to identify other comorbid factors for testing in multivariate models.

There was general consensus the HCT-CI, appropriately coded, is a powerful clinical tool, which may lead to risk-mitigating strategies at centers. Aside from its benefit in risk adjustment for survival modeling, it could be a useful tool for centers when considering transplant eligibility and decision-making regarding approach to HCT. This increases the value of training to improve its accurate collection and reporting.

Is the HCT-CI sufficiently accounting for co-morbidities in determining center-specific outcomes reporting?

<u>Recommendations:</u>

- CIBMTR should continue to collect the HCT-CI and use the information to adjust pre-transplant comorbid conditions in the center-specific survival analysis.

- CIBMTR should take measures, where possible, to improve reliability of reporting of the HCT-CI. Such measures may include:
    - Development and dissemination of specific guidelines for co-morbidity coding, so data acquisition is consistent among centers. These guidelines should have unambiguous definitions of comorbidities.
    - Provide training to improve reliability, including a session at the BMT Tandem Meetings after the guidelines are released.
    - Disseminate 'best practices' of approaches to HCT-CI data collection and reporting that increase reliability, such as integrating physician review into HCT CI coding.
    - Work with transplant centers to explore opportunities to develop HCT-CI coding tools into EMRs.
- Continue to collect an "other specify" comorbidity field for use in assessing reliability and appropriateness of comorbidity reporting at centers, and for use to identify potential new comorbidities for risk adjustment.
- CIBMTR should continue an active research program evaluating the HCT-CI and other comorbidities and their prognostic value in center-specific analyses. Trends in comorbidity scores over time should be evaluated. CIBMTR should consider re-factoring the HCT-CI once reliability of data reporting has improved.

DISEASE RISK INDEX FOR ALLOGENEIC HCT

What disease factors should be collected and used for adjustment?

The current center-specific analysis incorporates disease and disease status at transplant in the multivariate model. Clinically meaningful categories of disease and disease status are introduced into the model and tested for their effect on survival. Large sample sizes in the center-specific analysis allow for relatively discrete disease and disease-status groupings with regard to outcomes adjustment. CIBMTR re-evaluates the disease/disease status categories used in the center outcomes analysis annually.

A recent publication by Armand et al[11] re-evaluates disease and disease status categorization. The goal of their analysis is to develop a simple stratification tool to categorize allogeneic HCT patients into groups with different survival based on disease and disease status at transplant. This simple stratification system would then be used as the basis for adjustment for disease and disease status in studies with heterogeneous cohorts of transplant patients when disease outcomes are not the primary aim of the study. The methods and results of the study were presented.

A study to confirm the disease and disease stage using the risk categories defined by Armand is underway at the CIBMTR. Results of this study may be used to inform future disease risk adjustment in the center-specific survival analysis. Preliminary analyses of refined disease categorization based on non-Hodgkin lymphoma (NHL) subtypes were performed using the data available for the 2012 analysis. This refined disease categorization appears to provide better risk adjustment compared to a single category of 'NHL.' CIBMTR anticipates using more specific disease categorization for NHL

recipients in the 2013 report. Similarly, previous reports have categorized non-malignant diseases into Severe Aplastic Anemia and other non-malignant diseases. To further discriminate disease adjustment, CIBMTR tested dividing the non-malignant diseases into Fanconi Anemia, inherited erythrocyte abnormalities, inherited immune system disorders, inherited metabolic disorders, histiocytic disorders, and other non-malignant diseases. This disease categorization did improve the disease risk adjustment in the center-specific analysis, and was incorporated in the 2012 analysis.

Recommendations:

- Adopt the disease categorization for non-malignant diseases as described above.
- Continue to use the current disease categorizations, including for NHL, in the center-specific analysis. Re-evaluate disease and disease status categories, particularly for NHL, once the study to validate the 'disease risk index' proposed by Armand et al is complete.

TRANSPLANT ESSENTIAL DATA FORMS REVISION

What changes should the CIBMTR make to the TED-level forms to improve risk adjustment?

CIBMTR collects data at two different levels: Transplant Essential Data (TED) forms and Comprehensive Report Forms (CRFs). The TED form collects an internationally accepted standard data set that contains a relatively limited number of fields focusing on critical HCT variables. Participating CIBMTR centers must submit TED-level data for all consecutive HCT recipients. TED-level data, with some additional donor and graft characteristics, comprise the obligatory data required for U.S. centers under the Stem Cell Therapeutic and Research Act of 2005 (reauthorized in 2010).

TED-level data collection forms represent essential data necessary to understand basic characteristics of the recipient, their disease, the transplant procedure and outcomes. These data are useful for quality assurance efforts (and are the data expected by the Foundation for the Accreditation of Cellular Therapy (FACT) and the Joint Accreditation Committee-ISCT[1] & EBMT[2] (JACIE) to meet requirements for accreditation). These data are also collected to fulfill the reporting and analytic requirements of the Program. Therefore, it is important that the data collection forms obtain sufficient information not only to report transplant activities and trends but also to adequately perform risk adjustment in the center-specific survival analysis performed for the Program. Balancing the burden of data collection and reporting with the need to collect adequate data is a difficult but crucial component when considering which data to collect on the TED forms. Forms used to collect data for the Program must be approved by the Office of Management and Budget (OMB) in compliance with the Paperwork Reduction Act. Similarly, data elements must be straightforward, easily understood, reasonable to collect and report, and collected in a standard fashion by most if not all transplant centers.

[1] ISCT: International Society for Cellular Therapy
[2] EBMT: European Group for Blood and Marrow Transplantation

CIBMTR has been engaging the broad transplant community to revise its data collection forms in 2012. The TED-level data forms collected for the Program are among the forms being revised. Physicians, data professionals, metadata analysts and internal staff have participated in the process to ensure broad acceptance and relevance.

Because the data collected on the TED form are used to perform risk adjustment for center-specific analysis, the attendees at the Center Outcomes Forum were engaged to discuss updates to the pre-TED (pre-transplant data collection) form. Only changes relevant to center-specific outcomes reporting will be reviewed here.

Patient related factors:

The patient-related factors discussed largely involved comorbidity reporting (see previous section, HCT Co-Morbidity Index). There was broad acceptance and recommendation to continue collection of the HCT-CI, with enhanced guidance and training to improve data reporting. Questions were raised as to whether the data element pertaining to mechanical ventilation remains relevant, with confirmation from the group that this is a reasonably discrete data element that can be reported and is of value, particularly for use in pediatric immune deficiency diseases. Similarly, there has been increasing interest in prognostic value of laboratory values for ferritin, albumin, platelet count and c-reactive protein pre-transplant.

Disease-related factors:

Most discussion focused on collecting sufficient information to characterize disease-related risk for use in center outcomes reporting. Because leukemia is the most common indication for allogeneic HCT, capturing risk of recurrence is important. Discussion included suggestions to collect: relevant cytogenetics at diagnosis for acute myleogenous leukemia (AML), acute lymphoblastic leukemia (ALL), myelodysplastic syndrome (MDS), chronic lymphocytic leukemia (CLL) and multiple myeloma (MM); prognostic molecular markers; number of induction cycles to achieve most recent remission for acute leukemia; date of most recent relapse for acute leukemias beyond first remission at HCT; remission status defined by cytogenetic, flow cytometric or molecular markers beyond hematologic remission criteria; and use of PET scan results for lymphomas.

No specific recommendations regarding transplant-related factors were made.

Following discussion of the relative value of the suggested factors in predicting outcome, their general availability and effort of reporting, the following specific recommendations were made:

Recommendations:

- Include relevant prognostic cytogenetic abnormalities at any time before HCT for AML, ALL, MDS, and MM. Include question regarding 17p abnormalities in CLL at diagnosis.

- Collect relevant prognostic molecular markers at any time before HCT for AML and ALL.
- Collect components required for the International Prognostic Scoring System (IPSS) in MDS at diagnosis and before HCT.
- Include date of most recent relapse pre-HCT for leukemias.
- Include total number of inductions required to achieve the most recent remission as a discrete variable.
- Collect information for patients in hematologic complete remission (CR) at transplant regarding whether they were also in CR as determined by cytogenetic, flow cytometric or molecular criteria, if available.
- Incorporate PET scanning into the response/disease status criteria for the lymphomas.
- Continue to collect mechanical ventilation history.
- Eliminate basic fungal infection question.
- Collect ferritin on the Comprehensive Report forms (CRF) to support additional research.
- Consider addition of c-reactive protein and albumin pre-HCT to the CRF as future research supports their prognostic value.

CHARACTERISITICS OF CENTERS THAT AFFECT OUTCOMES PERFORMANCE

CIBMTR has an active research program exploring center-related characteristics that affect outcomes. One goal of this research is to identify characteristics that are associated with improved outcomes, such that this information can be used by centers for performance improvement efforts. Results were presented from two ongoing research projects. Both projects are supported by surveys of adult and pediatric transplant centers to define: individual medical center characteristics (location, teaching status, adult vs. pediatric); healthcare provider characteristics (e.g., number of transplant physicians/mid-level providers, ratios of transplant physicians/mid-level providers/nurses to patients); transplant program resources (e.g., center volume, number of beds for HCT); and care team structure.

The results of the adult transplant center survey conducted between March and July 2012 were described. Response rate to the survey was 79%. Characteristics reported by centers participating in the survey were described. More than 85% of the patients included in the center outcomes analysis for transplant years 2008-2010 had their transplants at centers performing more than 75 transplants annually. Most HCT programs are in academic teaching hospitals, and larger programs are more likely to participate in cooperative groups for clinical trials and have specific survivorship programs. Staffing by pharmacists, nursing and advanced practice providers is generally greater at larger facilities though staff to patient ratios vary substantially. Larger programs are more likely to use BMT-specific attending providers rather than attending physicians who split their responsibilities managing non-BMT patients. Analyses are expected to be completed by

the end of the calendar year and will be presented in an appropriate scientific forum and submitted for publication.

Preliminary results of the study evaluating pediatric transplant center characteristics and outcomes were also presented. Similar to the adult survey, response rates were 80%. Although some centers performed both pediatric and adult HCT, only outcomes of pediatric HCT were analyzed. Most (71%) centers had more than 15 years' experience performing HCT. The median number of inpatients per physician was five, and the median number of mid-level providers is two full-time equivalents. Other center characteristics were described. After adjusting for significant patient-, disease-, and transplant-related factors in multivariate models, three center-related characteristics were found to be associated with survival after HCT:

- Center volume in excess of 16 HCTs over a 2-year period is associated with better overall survival in the immediate post-transplant period.
- Attending physician to inpatient ratio in excess of 5 is associated with higher overall survival at day-100 and 1-year.
- Access to specialized care (out-patient transplant-specific clinic) on weekends is associated with higher overall survival at 1-year.

These data suggest that center experience, as manifest by volume of transplants, is associated with better survival, and is a potentially modifiable factor. Results of this study are being finalized for publication.

The results of these studies stimulated discussion among the group regarding measurement of provider volume, center volume and how their effects on HCT outcomes may be mediated. Volume may be a surrogate for other factors that affect outcomes. This was considered important since center volume may not be a readily modified factor, particularly at pediatric centers, and suggestions to use high-volume centers may have unintended consequences of driving patients and caregivers long distances from their support networks for care.

There was strong consensus that CIBMTR should continue to maintain an active research agenda into center-based factors that are associated with outcomes. Several suggestions were made for future research in this area, including further differentiation of volume effects.

<u>Recommendations:</u>

- Use modeling to determine whether center-based factors can predict the difference between observed and expected survival. Consider specific evaluation of factors associated with change in performance from 'under-performing' to 'as-expected' performance, or from 'as-expected' to 'above-expected' performance.
- Continue to collect information about centers' practices and patterns of care, including periodic surveys to identify factors associated with outcomes.
- Attempt to determine whether use of Good Manufacturing Practice facilities or in-house cell processing labs affects outcomes.

- Using data collected on future surveys, determine whether a meaningful and statistically significant cut-point exists for physician, advanced practice provider, and nursing staffing.
- Using data collected on future surveys, determine whether a minimal threshold of provider FTE devoted to patient care is associated with outcomes.
- Disseminate results regarding center-based practices associated with outcomes broadly, through both peer-reviewed publications and with center directors directly.

MAKING ADDITIONAL DATA AVAILABLE FOR CENTER'S PERFORMANCE IMPROVEMENT EFFORTS

A major objective of the center outcomes reporting process is to provide transplant centers with performance measures and tools that facilitate quality improvement initiatives. To achieve this, CIBMTR currently provides reports to center directors describing the patient-, disease- and transplant-related factors at the individual center with the combined demographics of all HCT in the US, sorted by conditioning intensity and type of transplant (related vs. unrelated). As well, data is provided for 100-day, 6-month and one-year survival for each center and for all HCTs in the US by year of HCT, sorted by the same criteria. These reports provide context for the individual center using normative national data.

CIBMTR may have the opportunity to provide individual centers with information that increases their understanding of outcomes in specific groups of patients and places these data in context beyond the information found in the center-specific survival analysis and univariate individual center descriptive reports. Even though these supplemental reports may not include multivariate adjusted outcomes or formal statistical comparisons, they provide important context for center directors to evaluate performance. There were numerous suggestions for reports that would be useful for center directors. It was noted that informing centers that are performing below average may be the best way to drive improvement.

Providing additional information for centers to use for performance could take several forms. Additional pre-defined descriptive reports with greater frequency, greater access to individual centers' data maintained by the CIBMTR, and enhanced reporting of research are three possible methods that can increase use of data by centers for performance improvement initiatives.

Several suggestions to provide additional descriptive reports were discussed. These include providing: normative outcome data for high-risk patients; information for other outcomes such as non-relapse mortality or graft vs. host disease; year-to-year same-center comparisons by particular risk groups for mortality; and interim reports for 100-day mortality. Pre-defined reports may be more important for small centers with fewer resources that can be devoted to quality improvement analyses.

Greater access to program-specific data through the CIBMTR may enhance centers' efforts to examine quality and determine outcomes of center-based quality initiatives. Much information is already available to centers via the Data Back To Centers application hosted on the CIBMTR website (www.cibmtr.org). Centers can use data reported to the CIBMTR and available for download to perform analyses beyond those completed by the CIBMTR to understand their outcomes. They can couple their data available from the CIBMTR with more specific patient-level data maintained by the center, such as bloodstream infection rates, care practices, provider level factors or other characteristics to identify associations with better outcomes. The ASBMT Committee on Quality Outcomes and the Information Technology Committee are considering recommendations to CIBMTR of ways to make more data available to small centers. There may be opportunities in the future to provide access to tools to analyze standard outcomes for each center director using their reported data.

Identification of high-quality programs, those whose performance is consistently above expected, provides an opportunity to determine factors which distinguish them from other centers. Similar opportunities may be afforded by studying centers whose performance improves over time. Part of the agenda of the health services research program is to identify factors that contribute to superior outcomes at such centers so that these factors can be generalized to other centers to broadly improve outcomes for all recipients. Aside from center-based research projects as outlined in the section "characteristics of centers that affect outcomes performance", CIBMTR's health services research program can consider site visits to attempt to identify program components associated with superior outcomes that may be adopted at other centers. Such site visits may also generate hypotheses that can be tested in future research projects.

Ideally, the tools available from CIBMTR for performance improvement will integrate with other quality initiatives that transplant centers undertake, such as FACT or Joint Commission on Accreditation of Healthcare (JCAHO) accreditation. However, JCAHO is interested in provider-specific information rather than program information. Although there may be interest in provider-specific information, it was acknowledged that data collection required to support such analyses is not readily achievable using reporting methods in place at the current time.

Recommendations:

- CIBMTR should continue to explore ways to provide additional data and reports for centers' use in performance improvement efforts. These efforts will enhance the value of the resource to centers, and improve incentives to provide high quality data to CIBMTR.
- CIBMTR should continue to improve completeness of data available to centers for use in quality assurance (QA) projects via the Data Back to Centers application.
- CIBMTR should continue to work with ASBMT Committee on Quality Outcomes and other stakeholders to identify specific enhancements to its supplemental center-specific reports for center directors to support their QA efforts.

HOW SHOULD THE RESULTS OF THE CENTER OUTCOMES REPORT BE PRESENTED?

How should the report be presented to achieve greatest comprehension?

The results of the center outcomes analysis are presented in a Transplant Center Directory which is available online at http://marrow.org/access and http://bloodcell.transplant.hrsa.gov. CIBMTR performs the analysis and, following approval of the final report by HRSA, makes it available to Be the Match® Patient Services (the Office of Patient Advocacy/Single Point of Access contractor) for online posting.

Feedback from patients indicates that the report in its current format is hard to find or understand. Limitations of the publicly available data include complex language and concepts that are difficult for many patients to understand, information spanning multiple linked websites, and provision of raw numeric data that does not account for censoring or follow-up. These limitations may cause the currently available data to be misunderstood or unintentionally misleading to some audiences.

There was considerable deliberation regarding the goals of making center-specific outcomes data available to the public. These goals, determined by HRSA, could include informing the public of anticipated outcomes, informing patients' choices regarding transplant centers, and driving improvements in performance by centers in response to public reporting.

Regardless of the specific objectives, CIBMTR and Be the Match Patient Services are interested in making the data as objective, accessible and readily understood by patients as possible.

Several of the suggestions and concerns raised at prior Center Outcomes Forums were re-visited. There was concern that statistical concepts such as observed survival, expected survival and confidence limits surrounding the latter are not understood by a lay audience, or easily explained (Appendix B). Patients may compare centers based upon differences between observed and predicted survival at each center, even when in all cases the observed survival falls within the confidence limits for predicted survival at those centers. Suggestions were made to improve explanations of statistical concepts. As well, a strong recommendation was made to remove the centers' predicted survival estimate from for the public report and instead just display the confidence interval which anchors the performance (the 95% confidence limit for predicted survival) for the center. Further detail could be accessible to patients who must first complete a basic tutorial online to improve comprehension of the concepts.

Overall center performance based upon one year of the center-specific analysis could be represented symbolically to portray center outcomes. Symbols represent a simplistic method to describe centers' performance compared to predicted, and have been suggested at the two previous center outcomes forums. A rating display based upon a number of stars, or based upon a Consumer Reports-like "filled circle" approach have been

suggested. Examples were discussed. There was concern, however, that symbols may be over-interpreted as "good, average or bad" and oversimplify patient decision making.

The current website provides a single performance rating for each center based upon aggregate one-year survival after adjusting for patient, disease and transplant factors. Patients are particularly interested in outcomes for their specific disease and wish to use such information to compare centers. Unfortunately, for most indications for transplant, there are insufficient numbers of cases to meaningfully evaluate center's performance on a disease-by-disease basis. Presenting comparative data in this setting would be highly misleading. The current display of data for the public includes raw numbers of patients alive at one year after transplant, divided by the actual number transplanted in the same time interval, in several relatively broad patient and disease categories (Appendix C). Participants in the Forum expressed concern that presenting these raw survival data by a limited number of disease type, disease stage and recipient age categories has a high risk of misleading users of the site. Limitations of this approach include: the numbers of recipients in each category are generally very small and therefore subject to wide confidence limits (though no confidence limits are presented); the categories are not sufficiently refined to exclude substantial variation in the risk of death for each group; all diseases are not represented; and a simple presentation of vital status at one year does not account for differences in time to death within the year.

One suggested approach would be to display national survival data for each disease, describe centers' recent experience with managing the disease, then the centers overall performance adjusted for all diseases, with the appropriate confidence intervals. Another suggestion was made to consider organizing center-specific outcomes by disease rather than by center. This approach would list outcomes by disease in a standardized fashion, and provide ratings of centers' performance for each disease. This approach is severely limited by the insufficient number of cases at most transplant centers to have meaningful confidence limits, similar to the limitations discussed for the current website.

Participants discussed the possibility of eliminating the presentation of actual numbers of patients surviving to one year after HCT in each disease/disease stage and age category on the website. Instead, it was suggested that only information on the numbers of patients who receive a transplant in those categories be presented.

As in prior years, attendees endorsed a concept of presenting data in a layered approach where very simple data is presented initially, with increasing degrees of complexity presented, together with educational materials, with subsequent deeper layers of information.

A concern was expressed that 95% confidence intervals permit substantial "latitude", particularly at smaller centers, when considering performance indicators for healthcare quality. A suggestion to use a more stringent confidence limit for quality measurement may be more appropriate, such as 97% or 99% confidence intervals. This may be considered a value judgment to emphasize quality; however, such a change is likely to have substantial unintended consequences. If the expectations for performance are too

high, there is real possibility that centers with lower performance may close inappropriately, which would adversely affect access to HCT. In general, attendees considered the 95% confidence limit approach to be appropriate.

Recommendations:

- Present only the predicted survival range, not the predicted survival estimate, to avoid confusion. Present the observed survival estimate and where it falls compared to the predicted survival confidence interval.
- Eliminate the presentation of actual patient survival numbers (at one year after HCT) from tables with categories of disease, disease state and age categories, and instead only present the numbers of patients who received a transplant in those categories.
- Thoroughly review the webpages displaying center-specific survival to provide a simplified explanatory page for statistical concepts.
- Re-evaluate use of symbols to represent center performance.
- Continue to work with payer, transplant center, and patient representatives to present useful information on the public website while avoiding information that could be misleading or easily misunderstood.
- Consider a "how to interpret" center outcomes reporting video to be displayed.
- Consider providing high-level data and requiring completion of a statistical tutorial in patient-accessible language before displaying the more detailed data to users.
- Consider adding an electronic "form" for patients to enter general information about disease or location as a starting point for providing customized information for patient reference.
- Offer access to survival rates separated by related and unrelated donors.
- Remove center address and phone number from the top level of display and place it in deeper layer for those with interest to 'request' via hyperlink.

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Appendix A: Attendees of Center-Specific Outcomes Analysis Forum

Name	Organization	Representation
Thomas Joseph, MPS, CAE	ASBMT	ASBMT / HCT Center
Bob Krawisz, MBA	ASBMT	ASBMT / HCT Center
Amin Alousi, MD	University of Texas M.D. Anderson Cancer Center	ASBMT Committee on Quality Outcomes
Helen Heslop, MD	Baylor College of Medicine	ASBMT Committee on Quality Outcomes
Vincent Ho, MD	Dana-Farber Cancer Institute	ASBMT Committee on Quality Outcomes
H. Kent Holland, MD	Blood and Marrow Transplant Group of Georgia	ASBMT Committee on Quality Outcomes
Roy Jones, MD, PhD	University of Texas M.D. Anderson Cancer Center	ASBMT Committee on Quality Outcomes
Jan Sirilla, RN, MSN	OSU James Cancer Hospital	ASBMT Committee on Quality Outcomes
Pintip Chitphakdithai, PhD	NMDP	CIBMTR
Chelsea Collins	CIBMTR/MCW	CIBMTR
Mary Eapen, MBBS, MS	CIBMTR/MCW	CIBMTR
Parameswaran Hari, MD, MS	CIBMTR/MCW	CIBMTR
Mary Horowitz, MD, MS	CIBMTR/MCW	CIBMTR
Roberta King, MPH	NMDP	CIBMTR
Navneet Majhail, MD, MS	NMDP	CIBMTR
Willis Navarro, MD	NMDP	CIBMTR
Marcelo Pasquini, MD, MS	CIBMTR/MCW	CIBMTR
Kristjan Paulson	CIBMTR/MCW	CIBMTR
J. Douglas Rizzo, MD, MS	CIBMTR/MCW	CIBMTR
Wael Saber, MD, MS	CIBMTR/MCW	CIBMTR
Ying Shan, MS	NMDP	CIBMTR
Stephen Spellman, MS	NMDP	CIBMTR
James Bowman, MD	HRSA, Division of Transplantation	Government Agency
Robert Hartzman, MD, Capt MC, USN (ret)	Naval Medical Research Center	Government Agency
Muneer Abidi, MD	Karmanos Cancer Institute	HCT Center
Michael Eckrich, MD, MPH	Levine Children's Hospital	HCT Center
Hugo Fernandez, MD	H. Lee Moffitt Cancer Center and Research Institute	HCT Center
Dennis Gastineau, MD	Mayo Clinic	HCT Center
Mitchell Horwitz, MD	Duke University	HCT Center
Stephanie Lee, MD	Fred Hutchinson Cancer Research Center	HCT Center
John Levine, MD, MS	University of Michigan	HCT Center
Eneida Nemecek, MD	Oregon Health & Science University	HCT Center
Michael Pulsipher, MD	University of Utah School of Medicine, Huntsman Cancer Institute	HCT Center
Mohammed Sorror, MD, MSc	Fred Hutchinson Cancer Research Center	HCT Center
John Klein, PhD	CIBMTR/MCW	MCW-Biostatistics
Brent Logan, PhD	CIBMTR/MCW	MCW-Biostatistics
Janet Brunner, PA-C	CIBMTR/MCW	Other attendees
Carol Doleysh	CIBMTR/MCW	Other attendees
Sandy Korman, MS	CIBMTR/MCW	Other attendees
Kitty Marquardt, RN, MS	CIBMTR/MCW	Other attendees
Waleska Perez, MPH	CIBMTR/MCW	Other attendees
D'Etta Waldoch, CMP	CIBMTR/MCW	Other attendees
Maureen Beaman	None	Patient Advocate
Jean Kanten	NMDP	Patient Advocate
Elizabeth Murphy, EdD, RN	NMDP	Patient Advocate
Jim Omel, MD	Education and Advocacy	Patient Advocate
Barry Schatz	Loyola University Med Center	Patient Advocate

Name	Organization	Representation
Stephen Crawford, MD	Cigna LifeSource Transplant Network	Payer Group
Stephanie Farnia, MPH	NMDP	Payer Group
Dennis Irwin, MD	OptumHealth	Payer Group
Adriana Mariani, RN, BSN, MPM	Cigna LifeSource Transplant Network	Payer Group
Wendy Marinkovich, RN, MPH	Blue Cross Blue Shield Association	Payer Group
Patricia Martin, RN, BSN	WellPoint, Inc.	Payer Group
Ted Gooley, PhD	Fred Hutchinson Cancer Research Center	Statistical Consultant

Appendix B: Explanation of center-specific analysis on current website

Center-Specific Analysis

This analysis is based on transplants performed from Jan. 1, 2007 through Dec. 31, 2009 using unrelated donors and transplants performed from Jan. 1, 2008 through Dec. 31, 2009 using related donors. It only includes patients who underwent their first allogeneic transplant within these respective time periods and who had at least 100-day follow-up.

1. This center reported survival status data for **89** patients.
2. The **actual one-year survival** of these patients was **70%**.
3. The **predicted one-year survival** was **67%** (with a 95% confidence limit that the predicted survival was between 58% and 77%).
4. This center's **actual** results are **similar to** the **predicted** range for this center.

For help with understanding these statistics, please see How to Understand Transplant Center Statistics.

Appendix C: Sample of current survival data display

Survival by Patient's Age, Disease Type and Stage after Related Donor Transplantation

This report is based on first related transplants performed between January 2008 and December 2010. It only includes patients with known survival status at one year post-transplant. In some cases, patients may have been alive at last reported follow-up that was less than one year - they have not been included in this report. The first number represents the number of patients alive at one year post transplant. The second number is a total number of transplanted patients in that particular group.

Diagnosis	0-9 Yrs	10-19 Yrs	20-29 Yrs	30-39 Yrs	40-49 Yrs	50-59 Yrs	60+ Yrs	Overall
Acute lymphoblastic leukemia in first complete remission	--	--	--	--	1/1	--	--	1/1
Acute myelogenous leukemia in first complete remission	--	--	--	1/2	0/1	3/3	1/2	5/8
Acute myelogenous leukemia in second complete remission	--	--	--	1/1	0/2	1/2	0/1	2/6
Acute myelogenous leukemia in third or higher complete remission, relapse, or primary induction failure	--	--	0/1	--	--	--	--	0/1
Chronic lymphocytic leukemia	--	--	--	--	1/1	1/1	1/1	3/3
Chronic myelogenous leukemia in accelerated phase or second chronic phase	--	--	--	--	--	1/1	--	1/1
Multiple myeloma / Plasma cell disorder	--	--	--	--	1/1	4/6	3/5	8/12
Myelodysplastic disorders - Other MDS	--	--	--	--	0/1	--	--	0/1
Myeloproliferative syndromes	--	--	--	--	--	1/1	--	1/1
Non-Hodgkin lymphoma	--	--	--	--	2/4	3/3	--	5/7
Severe aplastic anemia	--	--	1/1	--	--	0/1	--	1/2
Total	--	--	1/2	2/3	5/11	14/18	5/9	27/43