Summary and Recommendations of the 2025 Center Outcomes Forum Held on November 20, 2025

EXECUTIVE SUMMARY

The 2025 Center Outcomes Forum was held on November 20, 2025. The purpose is to review the current approach to the Center-Specific Survival Analysis (CSA) and to provide meaningful recommendations for potential inclusion in future reports. CIBMTR® (Center for International Blood and Marrow Transplant Research) invited representatives of the hematopoietic cell transplantation (HCT) community, the American Society for Transplantation and Cellular Therapy (ASTCT) Committee on Quality Outcomes, Foundation for the Accreditation of Cellular Therapy (FACT), NMDP, governmental funding agencies, patients, private payers, and statisticians.

Discussion focused on 3 key topics involving center-specific outcomes reporting:

- Risk adjustment for acute leukemia (Measurable Residual Disease (MRD) Task Force),
- Optimizing handling of comorbidities (adults and pediatrics), and
- Refining transplant-related factors in risk adjustment (Alternative Donors)

The main discussion and recommendations are briefly summarized in the following pages. Workgroup recommendations are carefully considered by CIBMTR for implementation with specific attention to feasibility, benefits and burdens of recommended changes to information collection.

Final recommendations include:

General recommendations

- Maintain focus on **risk adjustment quality** and **data completeness**; continue staged incorporation of new variables after feasibility and quality checks (particularly MRD).
- Publish executive and detailed summaries in the CIBMTR Center Outcomes Forum archives.
- Hold an educational session at Tandem ("Beyond the Report Card…", February 4).

ALL risk adjustment

- **Prioritize NGS MRD (ClonoSeq) fields** on the Transplant Essential Data (TED) form: MRD present (Y/N), tissue source (BM/PB), quantitative result (cells per million/clone count), LoD/LoQ;
- **If centers report NGS MRD results, other methods of testing for MRD in ALL do not need to be reported**
- Continue collecting **BCR-ABL PCR** (ratio to control) for patients with Ph+ ALL but prioritize NGS MRD for risk adjustment due to higher specificity.
- Retain MFC data collection fields but allow centers using ClonoSeq to report NGS alone.
- Provide **targeted training** for data professionals on interpretation of MRD testing, including ClonoSeq outputs (distinguish heavy-chain vs light-chain findings, residual sequence below LoD).
- Recommend centers create guidance for their data professionals for the specific MRD testing utilized by the center and most common external tests performed pre-referral.

AML risk adjustment

- Collect MRD by MFC on BM only, add **minimum performance fields** (events, sensitivity, # markers) at TED and comprehensive report form (CRF).
- **Collect MRD using PCR or NGS** from BM or PB for specific evidence-based **ELN markers** (FLT3-ITD, NPM1, RUNX1-RUNX1T1 or CBFB-MYH11), with **LoD/LoQ** and **quantitative** results per marker at TED level.
- Collect MRD using PCR or NGS from BM or PB for an expanded panel of molecular markers at the CRF level guided by ELN AML 2022[1].
- MRD using PCR or NGS should be collected as separate and distinct methods
- Request structured **PDF upload** of molecular (NGS or PCR)/MFC source reports for all patients to enable future automated / AI-assisted extraction and potentially reduce centers' abstraction burden.

Adult co-morbidities

- **Incorporate CHARM variables** for patients ≥60: **patient-reported KPS**, **hs-CRP**, **% weight loss**, **MOCA**, alongside **albumin**, **age**, **HCT-CI**. Develop **training** materials and pragmatic time windows (e.g., MOCA within 1–3 months pre-HCT if stable). Consider pilot roll-outs and ROI analysis on CSA fit before full adoption.
- **Adopt eGFR (CKD-EPI)** to define renal impairment in risk adjustment if validated, replacing creatinine ≥2.0.
- **Vitamin D**: Do not add to TED at this time; centers should continue clinical screening/repletion per local practice.

Pediatric co-morbidities

- **Use Youth HCT-CI** (malignant & non-malignant versions) for pediatric risk adjustment in CSA; continue analyses and validation studies.
- For patients with hemoglobinopathies, continue collecting **liver iron content** and **RBC transfusion dependence**; reassess completeness of **TR jet velocity** and streamline data collection fields with clearer guidance. Continue to test these variables for significance in the risk-adjustment model.

Alternative donors

- **Maintain donor-type adjustment**, but **refine categories** (e.g., matched sibling; matched unrelated; alternative donors subdivided into **7/8 MMUD**, **≤6/8 MMUD**, **haploidentical**, **cord blood**) while monitoring evolving outcomes. Potentially adjust donor categories annually after testing for between-category differences in odds-ratios.
- **Continue adjusting for donor age** where applicable (particularly unrelated donors), acknowledging its robust impact on survival.
- Conduct **sensitivity analyses** (with/without donor-type/age) in the center specific survival analysis annually; publish impacts on center classification to ensure transparency and community trust.

INTRODUCTION

To increase transparency and understanding of center outcomes reporting in HCT, CIBMTR began in 2008 to hold Center Outcomes Forums at least biannually. The Center for International Blood and Marrow Transplant Research (CIBMTR) invites representatives of the hematopoietic cell transplantation (HCT) community, including transplant physicians and center directors, the American Society for Transplantation and Cellular Therapy (ASTCT), the Foundation for the Accreditation of Cellular Therapy (FACT), governmental funding agencies, patients, private payers, and statisticians. The purpose is to review the current approach to the Center-Specific Survival Analysis (CSA) and to provide meaningful recommendations for potential inclusion in future reports. Summaries of these meetings and presentations are available on the CIBMTR website.

Workgroup recommendations are carefully considered by CIBMTR for implementation with specific attention to feasibility, benefits and burdens of recommended changes to information collection.

Participants included a broad range of invited stakeholder participants (Appendix A) and work group members (Appendix B) who presented recommendations. A summary of the group discussion and recommendations from this meeting follows.

OVERVIEW OF 2025 CSA

An important function of the Center Outcomes Forum is to review the CSA and provide recommendations for improvement. It is essential that CIBMTR continue to collect relevant and updated patient, disease and transplant characteristics for use in the risk-adjustment models. Additionally, because this publicly available report has a high impact for the HCT community, it is important to periodically review the statistical modeling methodology to maintain accountability and transparency. Details about the report methodology can be found on the CIBMTR website.

The 2025 CSA Report was reviewed.

Discussion summary

- **Purpose & scope.** Public reporting of center outcomes is a requirement of the Health Resources and Services Administration (HRSA) Stem Cell Therapeutic Outcome Database (SCTOD) contract. CIBMTR has designed the CSA to provide an equitable, scientifically sound performance measurement tool for centers to support quality improvement and accreditation, with public reporting to inform patients .
- **Methods.** The analysis includes one-year survival, using a fixed-effects logistic regression model with risk adjustment across patient, disease, and limited transplant variables; 95% confidence intervals are used to compare observed vs. predicted survival for centers with >90% one-year follow-up.
- **Results.** The 2025 analysis and report included US allogeneic transplants performed from 2021–2023. There were ~26,000 patients at 182 centers included. The performance distribution of centers was typical: ~87% performing as expected, ~8.5% below expected and ~4.5% above expected.
- **Model updates (2025).** The model is similar to 2024 except for:
    - Variable additions:
        - Pediatric comorbidity indices (malignant & non-malignant)
        - Pre-transplant platelet count
        - TP53 subgrouping in AML adverse risk
        - TP53-mutated myelodysplastic syndrome (MDS)

        - Viral infection within 60 days of HCT, for patients with disorders of immune system and histiocytic diseases.
    - Variable removed:
        - Prior cellular therapy for lymphoma (non-significant).
    - Measurable residual disease (MRD) for acute myeloid leukemia (AML)/acute lymphoblastic leukemia (ALL) **not** yet included due to data quality challenges.
    - The full list of variables tested in the 2025 CSA, and the variables included can be found in the 2025 report and the 2025 methodology.

Recommendations

- Maintain focus on **risk adjustment quality** and **data completeness**; continue staged incorporation of new variables after feasibility and quality checks (particularly MRD).
- Publish executive and detailed summaries in the CIBMTR Center Outcomes Forum archives.
- Hold an educational session at Tandem ("Beyond the Report Card…", February 4).

RISK ADJUSTMENT FOR ACUTE LEUKEMIA (MRD TASK FORCE)

Background:

The importance of Measurable Residual Disease (MRD) in predicting outcomes in ALL and AML is well established. Testing options for MRD continue to expand, and it is challenging for centers to accurately report complex MRD results. Discussion at previous Center Outcomes Forums revealed data professionals have difficulty distinguishing routine diagnostic clinical test results from purpose-specific MRD testing (e.g., flow cytometry results, diagnostic NGS panels). Some methods of MRD testing (e.g., NGS myeloid panels) require advanced knowledge to appropriately interpret results. Misunderstandings between routine disease testing and genuine MRD testing or misinterpretation of results could lead to inaccurate reporting of clinical remission status or MRD status. Substantial heterogeneity exists in the types of testing for MRD within and across HCT centers, adding further complexity to collection, interpretation and reporting of data. Nonetheless, the clinical importance of MRD for prognostication and use in risk adjustment warrants collection of these data.

In response to recommendations from previous Center Outcomes Forums, CIBMTR revised its data collection to improve the clarity and completeness of MRD status for AML and ALL before HCT. Unfortunately, CIBMTR has uncovered residual challenges as it has attempted to integrate these data into analyses to support observational studies and the CSA. CIBMTR MRD data currently show considerable heterogeneity (low rates of definitive high-sensitivity results; frequent discrepancies between modalities; ambiguous molecular reporting and free-text responses (driver vs. germline vs. CHIP)) and therefore limited utility for analyses. Analyses completed for LK21-01[2] found variable prognostic value of pre-transplant flow cytometry-based MRD across centers, likely reflecting differences in assay implementation, sensitivity, and center reporting practices. The challenges CIBMTR faces are well-recognized across the MRD reporting landscape and highlight the limited prognostic utility of current registry-reported MRD data.

To better address the challenges inherent in collecting MRD data for acute leukemia, CIBMTR formed a task force (Appendix B) to make recommendations for ALL and AML. The main goal of the task force was to advise CIBMTR about appropriate revisions to MRD data collection to improve interpretation and predictive value by establishing a minimum standard representing "high sensitivity" testing. Specifically:

- Assess the current state of MRD data collection and variable definitions within CIBMTR forms and datasets
- Identify key sources of heterogeneity and misclassification in reported MRD data
- Recommend standardized data elements and definitions for MRD testing and interpretation across leukemia subtypes based on current clinically recommended testing
- Propose revisions to CIBMTR forms and data collection workflows to improve accuracy and utility of MRD data
- Define an approach for stratifying or adjusting MRD data for analysis when different methodologies are used
- Prioritize feasibility and clinical relevance to ensure recommendations are implementable by centers of varying resources

The recommendations of the Task Force were presented to gain feedback from stakeholder communities that can be used to refine the approach.

Recommendations for MRD in ALL

The initial recommendations of the task force (Attachment A) included:

- Collection of high sensitivity methods used for MRD including multiparameter flow cytometry (MFC), polymerase chain reaction (PCR) and next-generation sequencing (NGS) before HCT, including distinguishing PCR from NGS testing
- For MFC, collect evidence of MRD (Y/N), level of detection, level of sensitivity and source of tissue
- For quantitative PCR, collect evidence of MRD (Y/N), level of detection and source of tissue for BCR-ABL transcripts for Ph+ ALL and KMT2A rearrangements
- For NGS for Ig/TCR gene re-arrangements, collect evidence of MRD (Y/N), assay used (e.g. Clonoseq, Invivoscribe, or other), level of detection and source of tissue.

Discussion summary

- **Evidence base.**
    - High-sensitivity NGS MRD (ClonoSeq) outperforms flow cytometry in sensitivity/specificity, predictive value for relapse, and clinical utility (early detection enabling interventions) across all types of ALL.
    - Threshold matters - prognostic association evident below ~10^{-6}; detailed quantitation strengthens risk stratification.
    - Pediatric and adult data consistently show superior discrimination with NGS vs. MFC; BCR-ABL PCR can be discordant and less specific compared with ClonoSeq in Ph+ ALL.
- **Operational realities.**
    - Only ~half of adult ALL cellular therapy patients in the ALL Consortium received ClonoSeq;
    - Many centers receive PDF results not integrated in the electronic medical record;
    - Data managers face complexity in abstracting multi-page reports and properly interpreting limit of detection (LoD)/limit of quantitation (LoQ) per-sequence (light vs. heavy chain issues).
- **Feasibility debate.** Suggestions to:
    - Capture only ClonoSeq when available (omit MFC to reduce redundancy) and retain option to report MFC or PCR fields when NGS is not available given uneven ClonoSeq access/utilization by centers.

- Require information about tissue source (bone marrow (BM) vs peripheral blood (PB)), assay sensitivity/LoD/LoQ, quantitative clone counts, and upload of the vendor report to mitigate misinterpretation.

Final Recommendations for ALL

- **Prioritize NGS MRD (ClonoSeq) fields** on the Transplant Essential Data (TED) form: MRD present (Y/N), tissue source (BM/PB), quantitative result (cells per million/clone count), LoD/LoQ;
- **If centers report NGS MRD results, other methods of testing for MRD in ALL do not need to be reported**
- Continue collecting **BCR-ABL PCR** (ratio to control) for patients with Ph+ ALL but prioritize NGS MRD for risk adjustment due to higher specificity.
- Retain MFC data collection fields but allow centers using ClonoSeq to report NGS alone.
- Provide **targeted training** for data professionals on interpretation of MRD testing, including ClonoSeq outputs (distinguish heavy-chain vs light-chain findings, residual sequence below LoD).
- Recommend centers create guidance for their data professionals for the specific MRD testing utilized by the center and most common external tests performed pre-referral.

Recommendations for MRD in AML

The initial recommendations of the task force (attachment B) included:

- Collection of high sensitivity methods used for MRD including MFC, and separate PCR and NGS for specific ELN risk-defining molecular markers[1] before HCT. PCR and NGS should be collected distinctly.
- For Multiparameter Flow Cytometry (MFC), collect evidence of MRD (Y/N) on BM only, level of detection, level of sensitivity, number of markers used and specific gating strategy
- For quantitative PCR, collect evidence of MRD (Y/N) with an expanded list of specific ELN risk-defining molecular markers, source of tissue and level of detection
- For NGS, similarly collect evidence or MRD (Y/N) with an expanded list of specific ELN risk-defining molecular markers, source of tissue and level of detection.
- Provide option to report NGS using Invivoscribe for FLT3-ITD and NPM1

Discussion summary

- Current CIBMTR comprehensive report forms (CRFs) combine PCR/NGS fields; pre-transplant MRD capture lacks detail (e.g., whether MRD was assessed, assay performance, gating strategy for multiparameter flow cytometry (MFC), event counts). LK21-01[2] showed limited prognostic utility of registry-reported flow MRD and significant center-level heterogeneity.
- Proposed revisions:
    - **MFC:** record events acquired, assay markers/#-colors, sensitivity (%), BM only; optional fields (anticoagulant, viability, hemodilution) deemed too burdensome at this time.
    - **Molecular MRD:** separate PCR and NGS; explicitly list European LeukemiaNet (ELN) risk-defining markers; capture LoD/LoQ for each assay and tissue source; include InVivoScribe NGS details for FLT3-ITD and NPM1, given strong evidence of outcome association.
- **Feasibility Debate:**
    - There was general agreement MRD data are valuable and improved MRD data will better inform analysis in studies and the CSA.
    - The group discussed significant challenges with interpreting complex MRD tests impacting data entry, feasibility of reporting and the quality of the data. Although this

may be particularly burdensome for data professionals, interpretation may not always be straightforward for physicians. Additional challenges that may affect the quality of data were discussed:
        - Vendor reports regarding operational test characteristics and results are heterogeneous
        - Testing methods for MRD may vary within a center, and even if individual centers standardize their MRD testing approach centers often receive heterogeneous MRD tests from outside organizations including pre-transplant
    - Instances of contradictory results between 2 different reported MRD tests may require adjudication
- **Solutions Proposed**:
    - Collect MRD for AML as a "clinician decision point" based on clinician judgement with simple identification of method
        - Concern was raised about relying on subjective interpretations in the absence of supporting evidence
        - There may be unintended consequences of using subjective data for risk adjustment in the CSA
    - Collect information about each center's "default" approach/assay characteristics for pre-HCT MRD testing centrally and use this information to support centers' determinations of reported MRD for patients
        - This approach would not lead to higher data quality/utility because it makes too many assumptions about testing at centers
        - Aside from logistic capabilities needed to maintain current information for each center, this would not be effective for MRD testing completed outside the HCT centers
    - Collect source document MRD reports as PDFs from centers and interpret the results centrally at CIBMTR
        - Although a project is underway at CIBMTR to use AI to interpret PDF results, this project is in early stages and is not yet proven to be effective.
        - There may be discordance between judgement of MRD at center compared to interpretation centrally at CIBMTR
        - The logistics of providing PDF reports within the data collection system are still associated with some burden at centers
    - Limit collection of MRD at the TED level to assays and markers that meet ELN AML evidence-based guidelines and collect an expanded panel of molecular markers at the CRF level guided by ELN AML 2022[1]:
        - MFC with specific test characteristics
        - NGS or PCR testing for FLT3-ITD, NPM1, RUNX1-RUNX1T1 or CBFB-MYH11
    - Once the updated approach to MRD data collection is finalized, provide in-person and online training modules for data professionals

Final Recommendations for AML

- Collect MRD by MFC on BM only, add **minimum performance fields** (events, sensitivity, # markers) at TED and CRF.
- **Collect MRD using PCR or NGS** from BM or PB for specific evidence-based **ELN markers** (FLT3-ITD, NPM1, RUNX1-RUNX1T1 or CBFB-MYH11), with **LoD/LoQ** and **quantitative** results per marker at TED level.

- Collect MRD using PCR or NGS from BM or PB for an expanded panel of molecular markers at the CRF level guided by ELN AML 2022[1].
- MRD using PCR or NGS should be collected as <u>separate and distinct</u> methods
- Request structured **PDF upload** of molecular (NGS or PCR)/MFC source reports for all patients to enable future automated / AI-assisted extraction and potentially reduce centers' abstraction burden.

<u>Adapting to ELN 2024 for AML</u>

Discussion summary & Recommendations

- There was limited time for this topic. The group noted intent to align MRD/molecular capture with ELN 2024 risk categories, especially around TP53, FLT3, NPM1. These suggestions will combine with the AML MRD recommendations above and subsequent form revisions.

OPTIMIZING HANDLING OF COMORBIDITIES (ADULTS AND PEDIATRICS)

Background

CIBMTR incorporates several variables in the current risk adjustment model to handle patient comorbidities. With recent publication of findings from BMT CTN 1704 (Composite Health Risk Assessment Model (CHARM))[3] and youth malignant and non-malignant Hematopoietic Cell Transplantation–Comorbidity Index (HCT-CI)[4,5], a workgroup was asked to consider current evidence and recommend potential refinements to information collected by CIBMTR to use for risk adjustment for adult and pediatric comorbidities in future CSA.

<u>Initial Recommendations</u>:
The workgroup was asked to address 3 primary questions. Responses and strength of recommendation were presented at the meeting.

- Are there data currently collected by CIBMTR that should be considered/tested in the model (that are not currently considered)?
    a. *Yes. Consider renal dysfunction by CKD-EPI[6]. (Moderate recommendation)*
- Is the approach taken in the 2025 analysis for pediatric comorbidity risk adjustment adequate/appropriate while awaiting further validation?
    a. *Yes (Strong recommendation)*
- What information most relevant to comorbidities (adult and/or pediatric) should CIBMTR begin to collect (or stop collecting) to inform future risk adjustment while considering the burden for centers?
    a. *Continue to collect CHARM covariates currently captured including albumin, HCT-CI, and age. (Strong recommendation)*
    b. *In patients 60 years and older, begin to collect CHARM covariates not currently captured, including (Strong recommendation):*
        i. *patient reported KPS*
        ii. *weight loss over one year*
        iii. *cognition by Montreal Cognitive Assessment (MOCA)*
        iv. *high sensitivity CRP.*
    c. *Develop CHARM score as a factor for each patient aged 60 years or older before allogeneic HCT. (Strong recommendation) This would allow external validation, testing,*

and integration of CHARM in center performance adjustment model for all older HCT recipients. The work group acknowledged support for appropriate training would be required to achieve this goal.

d. *Continue collecting comorbidity variables currently considered for pediatric recipients of HCT to calculate adapted HCT-CI scores for malignant and non-malignant pediatric diseases (Strong recommendation).*
e. *For thalassemia and hemoglobinopathy continue to test liver iron content and red cell transfusion dependence as cases may increase (moderate recommendation).*
f. *Other Considerations*
    i. *Consider collecting variables and testing CHARM among adult patients younger than 60 years old (weak recommendation). This would require collecting CHARM variables for all adult patients regardless of age.*
    ii. *Gait speed (4-meter walk) is a potential variable to collect (weak recommendation) given some results of its prognostic value and Age-Friendly CMS Hospital Inpatient Reporting requirements.*
    iii. *Vitamin D level is a variable to consider for both adult and pediatric patients given some evidence about its prognostic value (weak recommendation).*

Discussion summary

Adults (CHARM & renal function):

- Results of BMT CTN 1704[3] were reviewed outlining the patient-related factors included in the final multivariate models predicting 1-year non-relapse mortality (NRM). CHARM has also been shown to correlate with functional recovery (frailty/disability-free survival)[7]. Based on these results, the working group proposed adding several components of **CHARM** not already collected by CIBMTR: *patient-reported KPS, % weight loss over 12 months, MOCA cognitive screen*. CIBMTR already collects HCT-CI, age, albumin, and high-sensitivity CRP and optional reporting of MOCA.
- Several practical concerns were discussed.
    - Adoption of the full "CHARM" factors for use in the CSA may increase confidence in the risk adjustment model for older HCT recipients.
    - A small number of centers are routinely using MOCA
    - Patient reported KPS, weight loss in last 12 months and MOCA all require direct patient-reported responses or interaction with patients. There were questions about variability of administering and scoring of MOCA. Collection of MOCA requires standardizing assessments within 21 days of the HCT within and across centers to achieve consistency. If these data elements are added, CIBMTR was advised to develop standardized training modules to assist center data professionals.
    - A specific validation study for the CHARM factors is not planned, however the factors included in BMT CTN 1704 were selected for consideration based on strong prior data supporting their predictive value.
    - Participants stated substantial uncertainty about whether centers are adequately prepared to begin systematically collecting MOCA and whether the incremental benefit of the additional data collection and inclusion in CSA risk adjustment outweighs the burden for centers.
    - Since BMT CTN 1704 focused on first allogeneic recipients age 60 or older, there were suggestions to limit additional data collection to this cohort of patients if the information is added to CIBMTR data collection. Additionally, CIBMTR could consider

working with several centers to pilot data collection for MOCA, patient reported KPS and patient reported weight loss before adopting system-wide

- **Renal function:** The working group recommended replacing the renal dysfunction criteria of adult creatinine ≥2.0 found in the original HCT-CI with **estimated glomerular filtration rate (eGFR) (based on Chronic Kidney Disease Epidemiology Collaboration (CKD EPI) 2021)** <60 criteria to better classify renal impairment and improve clinical representation. Use of eGFR-based HCT-CI led to minimal impact on predictive performance for overall survival (OS) and NRM compared to the original HCT-CI (C-statistic for OS 0.6289 and 0.6277 respectively)[6]. CIBMTR currently collects pre-HCT glomerular filtration rate (GFR) as reported by the centers, however the HCT-CI assessment for renal dysfunction is based on the original HCT-CI using serum creatinine. A strong consensus for this change was not achieved.
- **Vitamin D:** Mixed evidence from observational studies suggest Vitamin D deficiency is associated with worse HCT outcomes. Prognostic impact is negated with repletion pre HCT and repletion is easily accomplished and believed to be commonly addressed. Since it is likely most centers are measuring and treating Vitamin D deficiency there was consensus the utility of collecting relevant data for use in risk adjustment is low.

Pediatrics (Youth HCT-CI):

- Pediatric providers underuse the traditional HCT-CI initially developed for adult populations. Pediatric-specific comorbidity indices developed by the CIBMTR[4,5] address limitations of applicability of the HCT-CI in pediatric populations[8].
- Youth-specific HCT-CI systems adapt definitions more appropriate for children (e.g., **GFR-based renal function**, prior **mechanical ventilation** as pulmonary surrogate for PFTs; **body mass index (BMI) percentiles** including underweight/obesity; infection history). This **reclassifies >50%** of children with HCT-CI=0 into higher risk strata and is more clinically relevant for malignant and non-malignant pediatric HCT.
- Validation studies have not been completed, CIBMTR is planning future studies.
- There was strong consensus to continue to use pediatric specific comorbidity indices for malignant and non-malignant disease for risk adjustment in the CSA while awaiting results of validation studies.

Final Recommendations

Adults

- **Incorporate CHARM variables** for patients ≥60: **patient-reported KPS**, **hs-CRP**, **% weight loss**, **MOCA**, alongside **albumin**, **age**, **HCT-CI**. Develop **training** materials and pragmatic time windows (e.g., MOCA within 1–3 months pre-HCT if stable). Consider pilot roll-outs and ROI analysis on CSA fit before full adoption.
- **Adopt eGFR (CKD-EPI)** to define renal impairment in risk adjustment if validated, replacing creatinine ≥2.0.
- **Vitamin D**: Do not add to TED at this time; centers should continue clinical screening/repletion per local practice.

Pediatrics

- **Use Youth HCT-CI** (malignant & non-malignant versions) for pediatric risk adjustment in CSA; continue analyses and validation studies.

- For patients with hemoglobinopathies, continue collecting **liver iron content** and **RBC transfusion dependence**; reassess completeness of **TR jet velocity** and streamline data collection fields with clearer guidance. Continue to test these variables for significance in the risk-adjustment model.

REFINING TRANSPLANT-RELATED FACTORS IN RISK ADJUSTMENT (ALTERNATIVE DONORS)

Background:

CIBMTR has carefully considered which transplant-related factors to include in the CSA risk adjustment model. Variation in centers' performance (1 year OS) may be due to variation in center quality practices (different treatment choices) or in patient/disease factors independent of quality (e.g. age, severity of illness). Risk adjustment at the person level in the context of center outcomes reporting is intended to account for differential 'case-mix' of patients at a given center, by adjusting the predicted 1-year OS to account for these characteristics. Risk adjustment is appropriate for factors independent of quality/center performance. However, adjusting for factors that are not independent of quality may serve to mask the impact of those factors on center quality/performance. Risk factors that represent center decisions/choices, such as preparative regimen and GVHD prophylaxis, have typically been excluded from the risk adjustment model.

Alternative donor options have been limited until recently and expected HCT outcomes using alternative donors were significantly worse. Because HCT using alternative donors was acknowledged as higher risk, centers may have avoided transplanting patients using alternative donors because of perceived negative consequences related to public reporting. This would adversely affect access for patients with less well-matched donors. To "protect" centers from lower performance ratings expected from selection of alternative donors (and therefore protect access to HCT for patients with limited donor choices), CIBMTR has been including HLA matching, donor and graft source as factors in the current risk adjustment model.

With recent improvements in outcomes of alternative donor HCT using post-transplant cyclophosphamide expanding availability of suitable donors, centers have better opportunities to prioritize donor choices. Considering these advances, CIBMTR sought discussion about future modification of risk adjustment for use of alternative donors.

Discussion summary

- **The evolving landscape of alternative donor transplantation was presented.**
    - Use of mismatched unrelated donors (MMUD) and haploidentical donors has risen significantly with widespread adoption of **post-transplant cyclophosphamide (PTCy) across donor types**;
    - Outcomes of HCT using haploidentical donors[9] or 7/8 MMUD donors are similar to **8/8 MUD**[10].
    - Disparities in access to HLA matched unrelated donors persist, with access being more limited in patients of non-European ancestry;
    - Comparative data suggest **subtle OS decrements** as HLA mismatch increases[11,12];
    - **Donor age** is a strong predictor of outcomes[13,14];
    - Results of HCT adult recipients using cord blood are reported to be inferior compared to adult donors with PTCy in some randomized trials and registry studies;

    - Pediatric/AYA patient biology and disease entities differ, potentially explaining more heterogeneous results of comparisons between UCB and other donor sources, using different GVHD prevention strategies.
- **Risk-adjustment question.**
    - Historically, CSA adjusted for donor type and match to avoid penalizing centers constrained by alternative donor availability. With modern practice convergence (PTCy), should donor choice now be treated as a **center decision (quality)** rather than a patient constraint?
    - Preliminary internal fit tests (QIC/QICU) of the CSA model showed small differences between inclusion and exclusion of HLA match/donor source/donor type in the risk adjustment model; excluding donor type/age changed performance for ~8 centers; many odds ratios near 1 suggest limited impact for most centers.
- **Stakeholder input.** Mixed views were outlined:
    - Some favored **not adjusting** donor choice (akin to current approach to preparative regimen/GVHD prophylaxis) to avoid masking center practice effects that impact center quality.
    - Others urged caution considering the ongoing evolution in alternative donor HCT, citing gaps between results from real-world studies vs trials using highly selected patients, and confounding by GVHD prophylaxis platforms;
    - There was more consensus around use of **refined categories of alternative donors** (keep cord blood and ≤6/8 MMUD distinct), retention of **donor age** effects.
    - There remain concerns risk-averse centers may choose to avoid use of alternative donors as an unintended consequence of changing the approach to risk adjustment

Final Recommendations

- **Maintain donor-type adjustment**, but **refine categories** (e.g., matched sibling; matched unrelated; alternative donors subdivided into **7/8 MMUD**, **≤6/8 MMUD**, **haploidentical**, **cord blood**) while monitoring evolving outcomes. Potentially adjust donor categories annually after testing for between-category differences in odds-ratios.
- **Continue adjusting for donor age** where applicable (particularly unrelated donors), acknowledging its robust impact on survival.
- Conduct **sensitivity analyses** (with/without donor-type/age) in the center specific survival analysis annually; publish impacts on center classification to ensure transparency and community trust.

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APPENDIX A: ATTENDEES OF 2023 CENTER OUTCOMES FORUM

Full Name	Organization	Representation	Registered	Attended
Stephanie Farnia, MPH	Nimitt Consulting	ASTCT	X	X
Dianna Howard, MD	Wake Forest Baptist Health	ASTCT QOC/HCT Ctr-Adult	X	X
Navneet Majhail, MD, MS	Sarah Cannon Transplant and Cellular Therapy Program at TriStar Centennial Medical Center	ASTCT QOC/HCT Ctr-Adult	X	X
Christopher Dandoy, MD	Cincinnati Children's Hospital Medical Center	ASTCT QOC/HCT Ctr-Peds	X	X
David Porter, MD	Abramson Cancer Center University of Pennsylvania Medical Center	ASTCT, HCT Ctr-Adult	X	X
Sumithira Vasu, MBBS, MD	Ohio State Medical Center, James Cancer Center	CIBMTR AC Chair, HCT Ctr-Adult	X	X
Jeffery Auletta, MD	CIBMTR - Minneapolis	CIBMTR ScD	X	X
Larisa Broglie, MD, MS	CIBMTR - Milwaukee	CIBMTR ScD	X	X
Steven Devine, MD	NMDP	CIBMTR ScD	X	X
Wasay Khan, MD, MS	CIBMTR - Milwaukee	CIBMTR ScD	X	X
J. Douglas Rizzo, MD, MS, FACP	CIBMTR - Milwaukee	CIBMTR ScD	X	X
Wael Saber, MD, MS	CIBMTR - Milwaukee	CIBMTR ScD	X	X
Bronwen Shaw, MD, PhD	CIBMTR - Milwaukee	CIBMTR ScD	X	X
Stephen Spellman, MBS	CIBMTR - Minneapolis	CIBMTR ScD	X	X
Patricia Steinert, PhD	CIBMTR - Milwaukee	CIBMTR ScD	X	X
Stephanie Larsen, RN MSN	Sarah Cannon Transplant and Cellular Therapy Program at TriStar Centennial Medical Center	Ctr Admin	X	X
Andrew Artz, MD, MS	City of Hope	HCT Ctr-Adult	X	X
Veronika Bachanova, MD, PhD	University of Minnesota Blood and Marrow Transplant Program - Adults	HCT Ctr-Adult	X	X
Firas El Chaer, MD	Miami Cancer Institute - per reg	HCT Ctr-Adult	X	X
Brian Friend, MD	Baylor College of Medicine Center for Cell and Gene Therapy	HCT Ctr-Adult	X	X
Nada Hamad, BSc, MSc, MBBS	St. Vincent's Hospital	HCT Ctr-Adult	X	X
Christopher Hourigan, MD, DPhil, FRCP	Virginia Tech	HCT Ctr-Adult	X	X
Reena Jayani-Kosarzycki, MD	Vanderbilt University Medical Center	HCT Ctr-Adult	X	X
Nandita Khera, MD, MPH	Mayo Clinic Arizona and Phoenix Children's Hospital	HCT Ctr-Adult	X	
Richard Maziarz, MD	Oregon Health and Science University	HCT Ctr-Adult	X	X
Shannon McCurdy, MD	Hospital of the University of Pennsylvania	HCT Ctr-Adult	X	X
Joseph McGuirk, DO	University of Kansas	HCT Ctr-Adult	X	X
Lori Muffly, MD	Stanford Health Care	HCT Ctr-Adult	X	X
Mariam Nawas, MD	University of Chicago	HCT Ctr-Adult	X	X

Full Name	Organization	Representation	Registered	Attended
Brian Shaffer, MD, MS	Memorial Sloan Kettering Cancer Center - Adults	HCT Ctr-Adult	X	X
Mohamed Sorror, MD, MSc	Fred Hutchinson Cancer Center	HCT Ctr-Adult	X	X
Amir Steinberg, MD	Westchester Medical Center	HCT Ctr-Adult	X	
Keith Stockerl-Goldstein, MD	Barnes Jewish Hospital	HCT Ctr-Adult	X	X
Christopher Strouse, MD	University of Iowa Hospitals & Clinics	HCT Ctr-Adult	X	X
Jesse Tettero, MD, PhD	Fralin Biomedical Research Institute at VTC	HCT Ctr-Adult	X	X
Sarah Wall, MD, MPH	Ohio State Medical Center, James Cancer Center	HCT Ctr-Adult	X	X
Edmund Waller, MD, PhD	Emory University Hospital	HCT Ctr-Adult	X	
Xinjie Xu, PhD, FACMG	Mayo Clinic Rochester	HCT Ctr-Adult	X	
Stella Davies, MD, PhD	Cincinnati Children's Hospital Medical Center	HCT Ctr-Peds	X	X
Akshay Sharma, MBBS	St. Jude Children's Research Hospital	HCT Ctr-Peds	X	
Monica Thakar, MD	Fred Hutchinson Cancer Center	HCT Ctr-Peds	X	X
Rebecca Higgins, APSW	Froedtert Memorial Lutheran Hospital	Patient Advocate	X	X
Anthony Bonagura, MD	Optum Health Services	Payer	X	X
Alberto Santos III, DO, MBA, MS	Aetna, Inc.	Payer	X	X
Michelle Williams, RN	BCBSA	Payer	X	X
James Bowman, MD MS FACS	Health Resources & Services Administration	Gov't staff (HRSA)	X	
Frank Holloman, MPA	Health Resources & Services Administration	Gov't staff (HRSA)	X	
Robert Johnson,	Health Resources & Services Administration	Gov't staff (HRSA)	X	X
Marilyn Levi, MD	Health Resources & Services Administration	Gov't staff (HRSA)	X	X
Carolyn Nganga-Good, DrPH, RN, CPH	Health Resources & Services Administration	Gov't staff (HRSA)	X	X
Nawraz Shawir, MBBS	Health Resources & Services Administration	Gov't staff (HRSA)	X	X
Kwang Woo Ahn, PhD	CIBMTR - Milwaukee	CIBMTR PhD Stats	X	X
Brent Logan, PhD	CIBMTR - Milwaukee	CIBMTR PhD Stats	X	X
Michael Martens, PhD	CIBMTR - Milwaukee	CIBMTR PhD Stats	X	
Kai Yang, PhD	CIBMTR - Milwaukee	CIBMTR PhD Stats	X	X
Jenni Bloomquist, MS, CSPO	CIBMTR - Minneapolis	NMDP Staff	X	X
Sue Logan, BS, CCRP	CIBMTR - Minneapolis	NMDP Staff	X	X
Mandi Proue, MPH	CIBMTR - Minneapolis	NMDP Staff	X	X
Katie Schoeppner, MSW, LICSW	NMDP	NMDP Staff	X	X
Ben Tweeten, MSW, LICSW	NMDP	NMDP Staff	X	X

Full Name	Organization	Representation	Registered	Attended
Maira Brey,	CIBMTR - Milwaukee	MCW Staff	X	X
Carol Doleysh,	CIBMTR - Milwaukee	MCW Staff	X	X
Alicia Halfmann,	CIBMTR - Milwaukee	MCW Staff	X	X
Cuyler Huffman, MS	CIBMTR - Milwaukee	MCW Staff	X	X
Wentong Liu, MS	CIBMTR - Milwaukee	MCW Staff	X	X
Dawn Lyons, BA	CIBMTR - Milwaukee	MCW Staff	X	X
Stephanie Meyers,	CIBMTR - Milwaukee	MCW Staff	X	X
Kelly Smith, MS	CIBMTR - Milwaukee	MCW Staff	X	X
Eileen Tuschl, DNP, RN, ACNS-BC, APNP	CIBMTR - Milwaukee	MCW Staff	X	X
Alexis Visotcky, MS	CIBMTR - Milwaukee	MCW Staff	X	X

APPENDIX B: WORK GROUP MEMBERS

Measurable residual disease in acute leukemia

Full Name	Organization	Representation
Veronika Bachanova, MD, PhD (chair)	University of Minnesota Blood and Marrow Transplant Program - Adults	HCT Ctr-Adult
Firas El Chaer, MD (chair)	Miami Cancer Institute - per reg	HCT Ctr-Adult
Lori Muffly, MD (chair)	Stanford Health Care	HCT Ctr-Adult
Jesse Tettero, MD, PhD (chair)	Fralin Biomedical Research Institute at VTC	HCT Ctr-Adult
Larisa Broglie, MD, MS	CIBMTR - Milwaukee	CIBMTR ScD
Steven Devine, MD	NMDP	CIBMTR ScD
Wasay Khan, MD, MS	CIBMTR - Milwaukee	CIBMTR ScD
Christopher Hourigan, MD, DPhil, FRCP	Virginia Tech	HCT Ctr-Adult
Xinjie Xu, PhD, FACMG	Mayo Clinic Rochester	HCT Ctr-Adult
Kwang Woo Ahn, PhD	CIBMTR - Milwaukee	CIBMTR PhD Stats
Wentong Liu, MS	CIBMTR - Milwaukee	MCW Staff
Eileen Tuschl, DNP, RN, ACNS-BC, APNP	CIBMTR - Milwaukee	MCW Staff

Comorbidity risk adjustment

Full Name	Organization	Representation
Andrew Artz, MD, MS (chair)	City of Hope	HCT Ctr-Adult
Mohamed Sorror, MD, MSc (chair)	Fred Hutchinson Cancer Center	HCT Ctr-Adult
Larisa Broglie, MD, MS	CIBMTR - Milwaukee	CIBMTR ScD
Brian Friend, MD	Baylor College of Medicine Center for Cell and Gene Therapy	HCT Ctr-Adult
Reena Jayani-Kosarzycki, MD	Vanderbilt University Medical Center	HCT Ctr-Adult
Nandita Khera, MD, MPH	Mayo Clinic Arizona and Phoenix Children's Hospital	HCT Ctr-Adult
Shannon McCurdy, MD	Hospital of the University of Pennsylvania	HCT Ctr-Adult
Mariam Nawas, MD	University of Chicago	HCT Ctr-Adult
Sarah Wall, MD, MPH	Ohio State Medical Center, James Cancer Center	HCT Ctr-Adult
Monica Thakar, MD	Fred Hutchinson Cancer Center	HCT Ctr-Peds