INTRODUCTION: The Summary Slides are an annual report on data submitted to the CIBMTR. This year, the slides are being posted online at www.cibmtr.org for easy accessibility, rather than published as part of the CIBMTR Newsletter. This change allowed us to combine parts I and II into one comprehensive set, updating the content in a format similar to previous years.

Slides 1 to 25 exhibit data on frequency of transplants according to age, donor and transplant type, graft source and disease, and early outcomes such as 100-day mortality by disease and transplant type. Slides 26 to 49 include overall survival outcomes according to disease, disease status, donor type, year of transplant and conditioning regimen intensity. Comparisons across survival curves are univariate and do not adjust for all potentially important factors; consequently, results should be interpreted cautiously.

Acute myeloid leukemia (AML), acute lymphocytic leukemia (ALL), and chronic myelogenous leukemia (CML) are classified as early disease (first complete remission [CR1] or first chronic phase [CP1]), intermediate (second or subsequent CR or CP or accelerated phase [AP]), or advanced (primary induction failure, active disease, or blastic phase) disease. Myelodysplastic syndrome (MDS) is divided into early [refractory anemia [RA] or refractory anemia with ringed sideroblasts [RARS]], or advanced (refractory anemia with excess of blasts [RAEB] or chronic myelomonocytic leukemia [CMML]) disease. Lymphoma is classified according to sensitivity to prior chemotherapy (chemosensitive or chemoresistant).

The classification of conditioning regimen intensity is based on the agents, doses and schedules used. Several classification systems are available, and for this report we used a composite classification. Cases defined as reduced-intensity by the transplant center were classified as such. Cases without such information and with available data on chemotherapy agents, radiation and doses, were classified according to the CIBMTR operational definition of conditioning regimen intensity:

- **Myeloablative conditioning regimen**: regimens with total body irradiation doses of ≥500 cGy, single fractionated doses of ≥800 cGy, busulfan doses of >9mg/kg, or melphalan doses of >150 mg/m² given as single agents or in combination with other drugs.
- **Reduced-intensity conditioning regimen**: regimens with lower doses of total body irradiation, fractionated radiation therapy, busulfan, and melphalan than those used to define a myeloablative conditioning regimen (above).

Slide 2: The CIBMTR database includes data reported by more than 500 centers in 54 countries worldwide.
Slide 3: Estimates of annual numbers of hematopoietic stem cell transplants worldwide, extrapolated from data compiled by the CIBMTR, European Blood and Marrow Transplant Group (EBMT), published reports from the Worldwide Network for Blood and Marrow Transplantation (WBMT) and the Asia Pacific Blood and Marrow Transplant Group (APBMT). Autologous transplant trends demonstrate changes in practice over time, with transplants for breast cancers in the early 1990s accounting for the majority of activity, and after 1999, lymphoproliferative disorders accounting for most of these transplants. The annual numbers of autologous transplants worldwide have continued to increase as a result of wider utilization of this treatment and its extension to recipients older than 60 years.

The numbers of allogeneic transplants have increased steadily over the past three decades. In the early 2000s, the increase in annual transplant numbers was slower than previous years, which is likely a result of a decrease in transplants performed for treating chronic myeloid leukemia (CML). This trend was mostly observed in countries classified by the World Bank as having high or intermediate-high gross national income. Subsequent trends in allogeneic transplant have shown a more rapid increase in annual numbers, which can be explained by higher number of unrelated donor transplants, older recipients being transplanted using reduced-intensity conditioning regimens, and the expanding utilization of umbilical cord blood.
Slide 4: Estimated annual numbers of transplants in the U.S. were compiled according to the number registered with CIBMTR. Estimates of how closely the numbers reported are representative of actual transplant activity vary according to the type of transplant and number of centers reporting data per year. Prior to 2007, all except unrelated donor allogeneic transplant facilitated by the NMDP were reported voluntarily. It was estimated that the CIBMTR captured 90% of all unrelated donor transplants performed in North America, 55 to 65% of related donor allogeneic transplants and 45 to 55% of autologous transplants. These estimates were extrapolated from other databases that capture transplant center activity, accreditation or hospital discharges. After 2007, the Stem Cell Transplant Outcomes Database (SCTOD) was initiated which changed reporting requirements and data capture to an electronic format. The SCTOD requires that all allogeneic transplants performed in the US be registered with CIBMTR. Data reporting of autologous transplants remains voluntary and the numbers in the CIBMTR database are estimated to be 55%. US numbers of allogeneic transplants in the CIBMTR are representative of the actual transplant activity.

The number of autologous transplants in the U.S. has steadily increased since 2000. Allogeneic transplants from unrelated donors surpassed the number of allogeneic transplants from related donors after 2007. The major contributing factors to this trend are the growth of unrelated donor databases and improvements in unrelated donor transplant.
Slide 5: Bone marrow is the primary graft source for transplantation in children, though the use of peripheral blood and umbilical cord blood grafts is increasing. During the period 2004 to 2008, peripheral blood accounted for 27% and cord blood accounted for 22% of allogeneic transplants in patients younger than 20. Among patients older than 20 years, peripheral blood is the most common source of allogeneic grafts. Use of umbilical cord grafts in patients >20 years, although infrequent, increased from 2 to 4% in the period from 2004 to 2008.
Slide 6: Mobilized peripheral blood progenitor cells are the most common graft source used in autologous transplants, accounting for 91% and 98% in children and adults, respectively, for the period from 2004 to 2008. The practice of combining bone marrow with peripheral blood progenitor cells in patients unable to mobilize optimal cell doses has decreased in both adults and children (<1%). Better mobilization regimens and patient selection may account for the rarity of this practice of late.
The number of autologous and allogeneic transplants for treatment of malignant diseases in older patients is increasing. Thirty-four percent of autologous transplant recipients and 12% of allogeneic transplant recipients in 2004-2008 were older than 60. The majority of autologous transplant recipients (65%) and 34% of allogeneic transplant recipient were older than 50 in this later period.
The proportion of patients treated for malignant diseases who are older than 50, and older than 60, after allogeneic and autologous transplants, respectively, has significantly increased in the last two decades. Improvements in supportive care, patient and donor selection, and the advent of reduced-intensity conditioning regimens for allogeneic transplants are the major contributors to this trend.
Slide 9: The most common indication for transplant was lymphoproliferative disorders (plasma cell disorders and lymphomas) in 2008, accounting for 60% of all transplants. Also in 2008, 52% of allogeneic transplants were performed for treatment of acute leukemias, and 45% of autologous transplants were performed for treatment of multiple myeloma.
In the pediatric population, allogeneic transplants are performed more often than autologous transplants. In 2008, allogeneic transplants performed in patients younger than 20 were for acute leukemias (50%) and non-malignant indications (36%). Autologous transplants were mostly performed for treatment of lymphoma and solid tumors in this patient population.

Slide 10: Indications for hematopoietic stem cell transplant for ages ≤20 years in North America 2008
Fifty-one percent of all transplants performed in North America in 2008 utilized alternative (unrelated) donors. Only about a third of the population has an HLA-matched sibling donor available for transplantation, which is among the greatest challenges for widespread application of this treatment. Expanding the unrelated donor pool and integrating different unrelated donor registries and cord blood banks have facilitated the procurement of alternative donors. The proportion of unrelated donor transplants is highest in transplants for leukemia, myelodysplasia and non-malignant diseases (other than aplastic anemia) (54%); and lowest among lymphoproliferative disorders and aplastic anemia (40%).
Slide 12: Annual numbers for unrelated donor transplants have increased in the last two decades for patients younger than 21. Transplants with umbilical cord blood have contributed significantly to this trend during the last decade. In 2007 and 2008, 46% of all unrelated donor transplants utilized umbilical cord blood grafts for this patient population.
Among patients older than 20, there has also been an increase in the number of alternative donor transplants. Mobilized peripheral blood progenitor cells is the most common graft source for unrelated donor transplants in this age group. Umbilical cord blood use in these patients is low, but is increasing steadily.
Slide 14: Comparison of unrelated donor graft sources between patients 20 years or less and patients older than 20 demonstrates that, in the period from 2004 to 2008, bone marrow was no longer the most common graft source. Umbilical cord blood was the most common graft source for patients 20 years or less (41%), and mobilized peripheral blood (70%) was the most common graft source for unrelated donor transplants in patients older than 20 during this period.
Slide 15: Umbilical cord blood transplants have better outcomes using cords that have more HLA matches and larger cell numbers. The limited number of cells in many cords limits widespread utilization of this graft source for heavier patients. However, the number of umbilical cord blood transplants performed in patients older than 16 years has steadily increased in the last decade, reaching 45% of all transplants that used this graft source in 2008. This trend may be explained by the larger pool of umbilical cord units to choose from, permitting selection units with larger cell doses and fewer HLA mismatches, or by approaches that utilize two units for one recipient.
One-year survival after myeloablative conditioning for acute leukemias in any remission phase, CML or MDS, age <50 years, by year of transplant and graft source, 1988-2008

Slide 16: One-year survival rates after transplantation have generally improved over the last two decades. Outcomes of unrelated donor transplants are approaching the rates of related donor transplants. Overall survival rates at one year are 74% (related donor) and 65% (unrelated donor) for these transplants in 2008. Improvements in HLA-matching techniques with consequently better donor selection, better overall patient selection for transplantation, and improvements in supportive care are the likely explanations for this trend.
Slide 17: The 100-day mortality rate is often cited to reflect the toxicity of the transplantation process. Autologous transplants have a much lower rate of 100-day mortality than allogeneic transplants. The primary disease and the disease status at the time of transplantation significantly affect early post-transplant mortality.
Slides 18-20: The effect of disease stage is even more apparent for allogeneic transplants. Patients receiving an HLA-identical sibling transplant for AML in remission have a 100-day mortality rate of 7 to 9%, compared to 22% for patients with active leukemia at the time of transplantation. Early mortality after an unrelated donor transplant is higher than after an HLA-identical sibling transplantation, but the rate also depends on the disease and disease stage. The causes of death in the first 100 days post-transplant mainly relate to the primary disease, graft-versus-host disease, infection and end-organ damage. After an autologous transplant, primary disease is the most commonly reported cause of death. Among allogeneic transplant recipients, unrelated donor transplants have fewer deaths related to the primary disease, however organ failure and infections are higher after unrelated donor transplants.
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Slide 21: Harnessing the graft-versus-tumor effect and decreasing upfront toxicity related to the conditioning regimen are the objectives when reduced-intensity conditioning regimens are used in allogeneic transplant for malignant diseases. The number of transplants using reduced-intensity conditioning has steadily increased in the last decade, mainly for patients 50 and older.
Slide 22: Among transplants with reduced-intensity conditioning, the use of alternative donors has also increased. The combination of umbilical cord blood grafts and reduced-intensity conditioning is relatively novel. Although it represents a minority of reduced intensity transplants, this approach is being used more frequently as umbilical cord blood graft use in adults increases.
The annual number of transplants for treating various malignant diseases and aplastic anemia has generally remain constant, except for chronic myeloid leukemia (CML) and acute myeloid leukemia (AML). Tyrosine kinase inhibitors are the first line of treatment for CML and allogeneic transplant is used in patients who have failed to respond to this treatment. The number of transplants for CML has dropped from approximately 2,000 per year to less than 500 per year in the last decade. Transplants for AML have increased, which is attributed to the increasing number of transplants with reduced-intensity conditioning. This allows patients who were previously ineligible for an allogeneic transplant due to age or comorbidities to undergo this treatment.
Slide 24: A major prognostic factor for survival in transplants for malignant diseases is the disease status at the time of transplant. The majority of transplants for AML are performed in patients in first complete remission (CR); but the proportion of patients with AML in second or later CR receiving an allogeneic transplant has increased in the period.
Slide 25: For patients with acute lymphocytic leukemia (ALL), transplantation is performed less frequently for patients with an active disease status. Early in the decade, transplants for ALL in second CR or higher were performed more frequently, however, there was a shift towards performing transplants earlier in the course of the disease as the decade went on. The increasing availability of alternative donors for adults is likely responsible for this shift in practices.
Slides 26-27: The CIBMTR has data for 21,388 patients receiving an HLA-matched sibling (n=11,714) or unrelated donor (n=9,674) transplant for AML between 1998 and 2008. Their disease status at the time of transplant and the donor type are the major predictors of post-transplant survival. The 3-year probabilities of survival after HLA-matched sibling transplant in this cohort was 59% ± 1%, 49% ± 1%, and 25% ± 1% for patients with early, intermediate, and advanced disease, respectively. The probabilities of survival after an unrelated donor transplant were 45% ± 1%, 43%± 1%, and 20% ± 1% for patients with early, intermediate, and advanced disease, respectively.
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Slide 28: Among 1,978 patients younger than 20 with AML, the 3-year probabilities of survival following transplant for early, intermediate, and advanced disease were 66% ± 1%, 56% ± 3%, and 38% ± 3%, respectively.
Slides 29-30: The 3-year probabilities of survival for the 2,077 patients with AML who received a transplant from 1998 to 2008 with a reduced-intensity conditioning regimen from an HLA-matched sibling donor were 49% ± 2%, 43% ± 3%, and 21% ± 2% for patients with early, intermediate, and advanced disease, respectively. The probabilities of survival for the 1,769 patients with AML who received an unrelated donor transplant were 40% ± 2%, 35% ± 2%, and 21% ± 2% for patients with early, intermediate and advanced disease, respectively.
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Slide 31: The CIBMTR has data for 3,309 autologous transplants performed for patients with AML between 1998 and 2008. Autologous transplants are rarely performed in patients with active AML. The 3-year probabilities of survival for patients with early, intermediate and advanced AML were 50% ± 1%, 50% ± 2%, and 21% ± 3%, respectively.
Slides 32-33: Allogeneic transplant is a potentially curative treatment for myelodysplastic syndrome (MDS). Outcomes differ according to the recipient’s age and disease status at the time of transplant, as well as by donor type. Among 177 recipients of an HLA-matched allogeneic transplant younger than 20, the 3-year probabilities of survival were 65% ± 6% and 63% ± 5% for patients with early and advanced disease, respectively. The corresponding probabilities of survival in the 331 recipients receiving an unrelated donor transplant were 63% ± 4% and 47% ± 4%. Among the 1,836 patients ≥20 years receiving an HLA-matched sibling transplant, the 3-year probabilities of survival were 50% ± 2% and 41% ± 2% for early and advanced MDS, respectively. The corresponding probabilities in the 1,651 older patients receiving an unrelated donor transplant were 44% ± 2% and 32% ± 2%.
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The median age of patients at diagnosis with MDS is 70 years, limiting the use of myeloablative conditioning regimens for most patients with this disease. Reduced-intensity conditioning regimens are increasingly used for allogeneic transplantation in MDS. Among 1,168 patients who underwent reduced-intensity conditioning allogeneic transplantation for MDS from 1998 to 2008, the 3-year survival probabilities for recipients of HLA-matched donor transplants (N=583) were 45% ± 4% and 41% ± 3% for early and advanced MDS, respectively. The corresponding probabilities for recipients of unrelated donor transplants (N=585) were 42% ± 4% and 28% ± 3.
Slides 35-36: Among young patients with ALL, for whom chemotherapy has a high success rate, allogeneic transplantation is generally reserved for patients with high-risk disease (i.e. high leukocyte count at diagnosis and the presence of poor-risk cytogenetic markers), who fail to achieve remission or who relapse after chemotherapy. Among the 2,471 patients younger than 20 receiving an HLA-matched sibling transplant, the 3-year probabilities of survival were 63% ± 2%, 54% ± 2%, and 26% ± 3% for patients with early, intermediate, and advanced disease, respectively. The corresponding probabilities of survival among the 3,212 recipients of an unrelated donor transplant were 55% ± 2%, 44% ± 1%, and 24% ± 2%.
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Slides 37-38: Older age at disease onset is a high-risk factor in ALL. Consequently, a larger proportion of ALL patients 20 or older undergo an allogeneic transplant early in the disease process. Among 3,409 patients ≥20 years of age receiving an HLA-matched sibling transplant, the 3-year survival probabilities were 49% ± 1%, 34% ± 2%, and 20% ± 2% for patients with early, intermediate, and advanced disease, respectively. Corresponding probabilities among the 3,081 recipients of an unrelated donor transplant were 43% ± 2%, 32% ± 2%, and 15% ± 2%.
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Slide 39: The CIBMTR has data for 5,329 HLA-matched sibling donor transplants for CML patients in chronic phase (CP, n=4,714) and in accelerated phase (AP, n=615) between 1998 and 2008. Among patients in CP, the 3-year probabilities of survival were 69% ± 1% for the period 1998 to 2000, and 71% ± 1% for transplants in performed from 2001 to 2008. Corresponding 3-year survival probabilities for patients in AP were 45% ± 3% and 56% ± 3%.
Both autologous and allogeneic transplants are treatment options for chronic lymphocytic leukemia (CLL) patients who fail standard chemotherapy or have high-risk features (e.g., cytogenetic abnormalities). The use of reduced-intensity conditioning regimens for allogeneic transplant continues to increase in this population. Among the 1,536 patients who underwent transplantation for CLL, the 3-year probabilities of survival were 77% ± 2% after autologous transplant, 51% ± 3% after an HLA-matched sibling transplant with a myeloablative conditioning regimen, and 58% ± 2% after an HLA-matched sibling transplant with a reduced-intensity conditioning regimen.


**Slide 41:** Allogeneic transplant is the treatment of choice for young patients with severe aplastic anemia and who have an HLA-matched sibling donor available. Among the 2,796 patients receiving an HLA-matched transplant for severe aplastic anemia between 1998 and 2008, the 3-year probabilities of survival were 86% ± 1% for those younger than 20, and 74% ± 1% for those 20 years of age or older. Among the 1,094 recipients of an unrelated donor transplant, the corresponding probabilities of survival were 65% ± 2% and 56% ± 2%.
Slide 42: Transplantation for Hodgkin disease (HD) is indicated in patients who have failed initial chemotherapy or radiation therapy. Survival after transplant for HD depends on disease response to previous salvage therapy. Among the 6,373 patients receiving an autologous transplant for HD between 1998 and 2008, the 3-year probabilities of survival were 82% ± 1%, 70% ± 1%, and 51% ± 2% for patients in complete remission, in partial remission, and with chemoresistant disease, respectively.
Slide 43: HD is an infrequent indication for allogeneic transplant and generally performed only in patients who experience disease relapse after receiving multiple lines of therapy or who have refractory disease and an available HLA-matched donor. The use of reduced-intensity conditioning regimens in these heavily pretreated patients allows for a graft-versus-lymphoma effect with less regimen-related toxicity. Among 343 patients receiving HLA-matched transplant for HD between 1998 and 2008, the 3-year probabilities of survival were 38% ± 4% with a myeloablative conditioning regimen and 43% ± 5% with a reduced-intensity conditioning regimen. The corresponding probabilities of survival in the 181 recipients of an unrelated donor transplant were 32% ± 6% and 41% ± 6%.
Slides 44-45: Transplantation for follicular lymphoma (FL) is generally reserved for patients with recurrent or aggressive disease, and autologous transplantation is the most common approach. Among the 2,155 patients receiving an autologous transplant for FL between 2000 and 2008, most had chemosensitive disease. The 3-year probabilities of survival were 74% ± 1% and 56% ± 4% for patients with chemosensitive and chemoresistant disease, respectively. Similar to CLL and HD, the use of reduced-intensity conditioning regimens is increasing for patients with FL. Among 888 patients with FL undergoing an HLA-matched sibling donor transplantation between 1998 and 2008, the 3-year probabilities of survival for patients with chemosensitive disease (N=731) were 67% ± 3% and 71% ± 2% for those receiving myeloablative and reduced-intensity conditioning regimens, respectively. Corresponding probabilities in the 149 patients with chemoresistant FL were 64% ± 6% and 60% ± 7%.
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Slides 46-47: Autologous transplants are an accepted treatment indication for diffuse large B-cell lymphoma (DLBCL) and, similar to FL, most autologous transplants are performed in patients with chemosensitive disease. Among the 6,650 patients who received an autologous transplant for DLBCL between 2000 and 2008, the 3-year probabilities of survival were 62% ± 1% and 36% ± 3% for patients with chemosensitive and chemoresistant disease, respectively. Allogeneic transplant for treatment of DLBCL is performed less frequently than for FL, and is generally used only in patients with aggressive disease that has been resistant to previous therapies, including autologous transplants. Among the 578 patients who underwent an HLA-matched sibling transplant for DLBCL from 1998 to 2008, the 3-year probabilities of survival for patients with chemosensitive disease (N=437) were 39% ± 3% and 46% ± 5% for patients receiving myeloablative and reduced-intensity conditioning regimens, respectively. The corresponding probabilities in the 141 patients with chemoresistant DLBCL were 21% ± 5% and 20% ± 7%.
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Slide 48: The optimal timing of transplant for mantle cell lymphoma (MCL) is not well defined. As with other mature B-cell lymphoproliferative disorders, autologous transplantation is the most common transplant approach. Among the 2,390 patients who received an autologous transplant for MCL between 1998 and 2008, the 3-year probability of survival was 69% ± 1%. Among 791 patients who underwent an allogeneic transplantation for MCL during the same period, the 3-year probabilities of survival for HLA-matched sibling donor transplants (N=513) were 53% ± 3%, and 55% ± 4% for patients receiving myeloablative and reduced-intensity conditioning regimens, respectively. Corresponding probabilities for unrelated donor transplantation (N=278) were 42% ± 6% and 43% ± 4%.
Slide 49: Multiple myeloma (MM) is the most common indication for an autologous transplant. Among 22,254 patients who received a single autologous transplant for MM between 1998 and 2008, the 3-year probability of survival was 68% ± 1%. Allogeneic transplantation for MM is reserved for patients with high risk disease, and the majority are performed after an autologous transplant with reduced-intensity or nonmyeloablative conditioning regimens. Among the 1,021 patients who received an allogeneic transplant for MM from 1998 to 2008, the 3-year probabilities of survival were 47% ± 2% for the 878 recipients of HLA-matched sibling donor transplants and 28% ± 4% for the 143 recipients of unrelated donor transplants.