Appendix G: CIBMTR Summary Slides

Current Uses and Outcomes of Hematopoietic Stem Cell Transplantation 2009: Summary Slides

INTRODUCTION: The Summary Slides are an annual report on data submitted to the CIBMTR. The first half focuses on trends in the use of hematopoietic cell transplantation (HCT) according to donor type, graft sources, patient age and transplant regimes. Early outcomes such as mortality rates at day 100 post HCT and causes of death are also included in this series. Graphs with total transplant numbers (slides 7 & 8) are estimates based on data reported to the CIBMTR adjusted according to transplant type. These adjustment factors are derived from comparisons with other national and international databases.

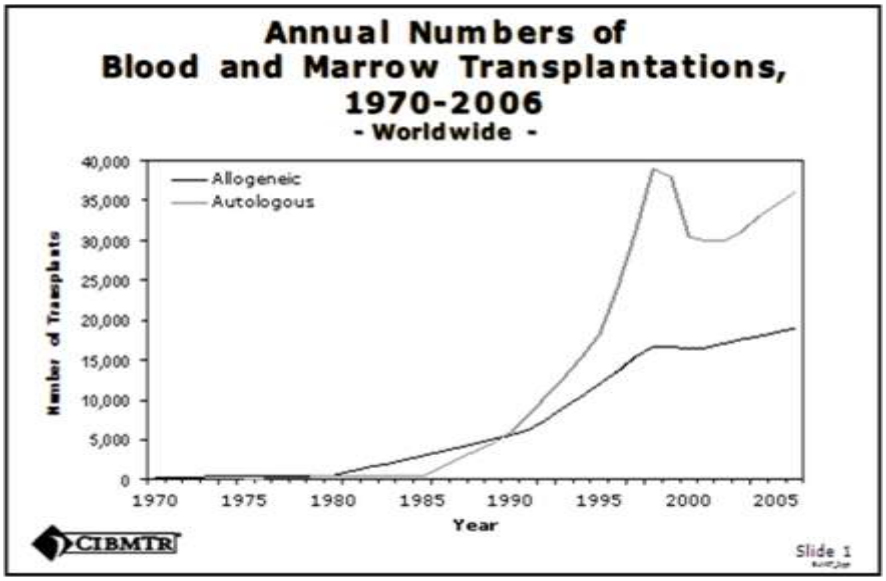
- Acute myeloid leukemia (AML), acute lymphocytic leukemia (ALL), and chronic myelogenous leukemia (CML) are classified as early (first complete remission [CR1] or first chronic phase [CP1]), intermediate (second or subsequent CR or CP or accelerated phase [AP]), and advanced (primary induction failure, active disease, or blastic phase) disease.
- Myelodysplastic syndrome (MDS) is divided into early (refractory anemia [RA] or refractory anemia with ringed sideroblasts [RARS]), and 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 intensities is based on the agents, doses and schedules used. Several classifications 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:

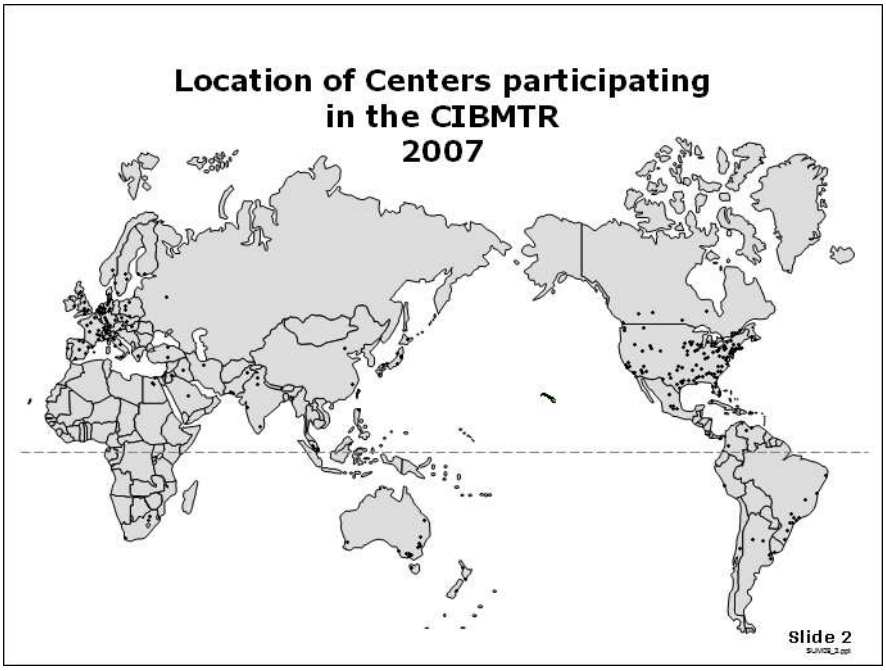
- Myeloablative conditioning regimen: regimens with total body irradiation doses of ≥500 cGY, single fractionated doses of ≥800 cGY, busulfan doses of >9mg/kg, or melphalan doses of >150 mg/m2 given as single agents or in combination with other drugs.
- Reduced-intensity conditioning regimen: regimens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

The second half of the CIBMTR summary slides describes the probabilities of survival in patients with diseases most commonly treated with HCT. The data were derived from patients transplanted between 1998 and 2007 and reported to CIBMTR. Survival curves are stratified by several factors: recipient age, donor type (i.e. autologous, human leukocyte antigen [HLA]-identical sibling, or matched-unrelated donor transplant), time from diagnosis to HCT, disease status or chemosensitivity at time of transplantation, and conditioning regimen intensity. However, all comparisons are univariate and do not adjust for other potentially important factors that may impact overall survival. Consequently, differences in outcomes between curves should be interpreted cautiously.

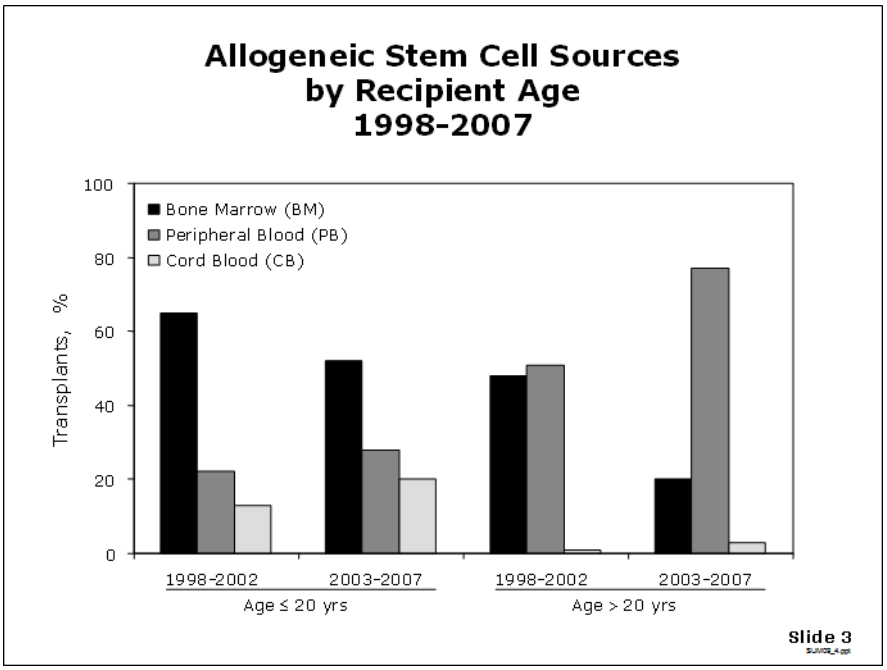
Pasquini MC, Wang Z. Current use and outcomes of hematopoietic stem cell transplantation: CIBMTR summary slides, 2009. CIBMTR Newsletter. Available at: http://www.cibmtr.org/PUBLICATIONS/Newsletter/index.html.



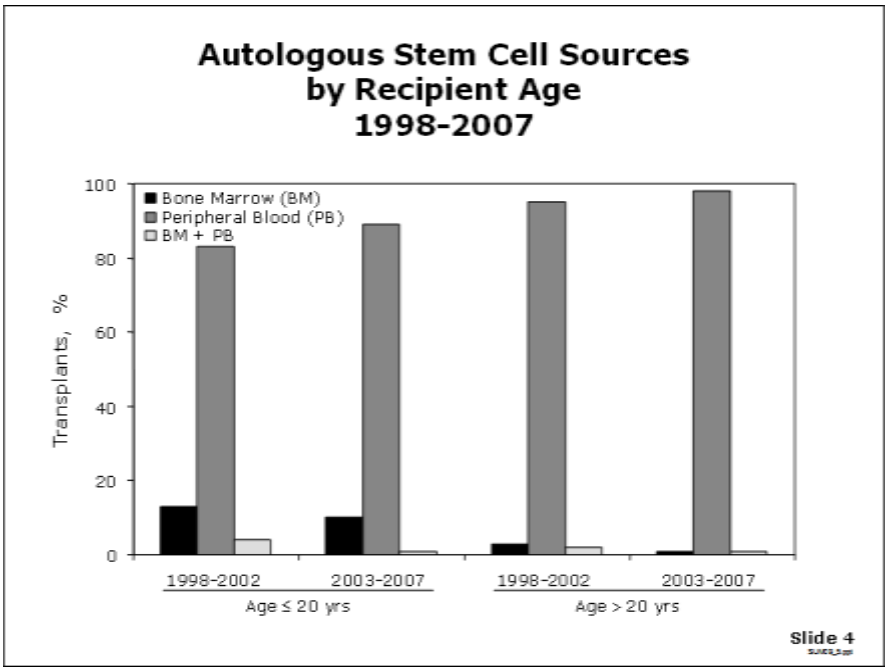
Slide 1: There are an estimated 50,000-60,000 hematopoietic stem cell transplants (HCTs) done every year worldwide. This slide shows several of the notable events in the field over the past decade. They include the initial enthusiasm and later disappointment about the use of autologous transplants for breast cancer, the availability of targeted non-transplant therapy for chronic myelogenous leukemia (a leading use for allogeneic HCT), and the increasing use of autologous and allogeneic HCT in older patients.



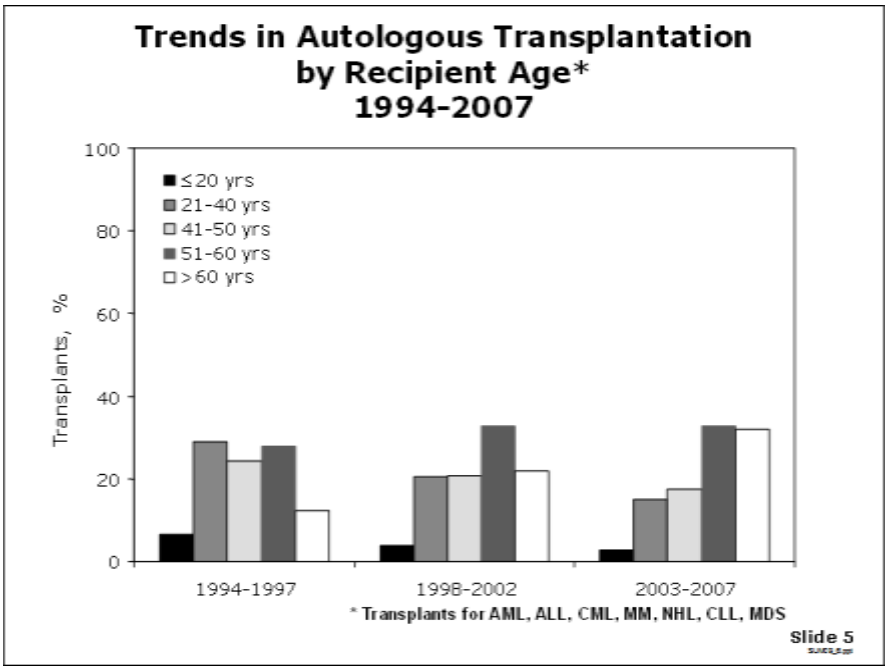
Slide 2: The CIBMTR database includes data reported by more than 500 centers in 54 countries worldwide.



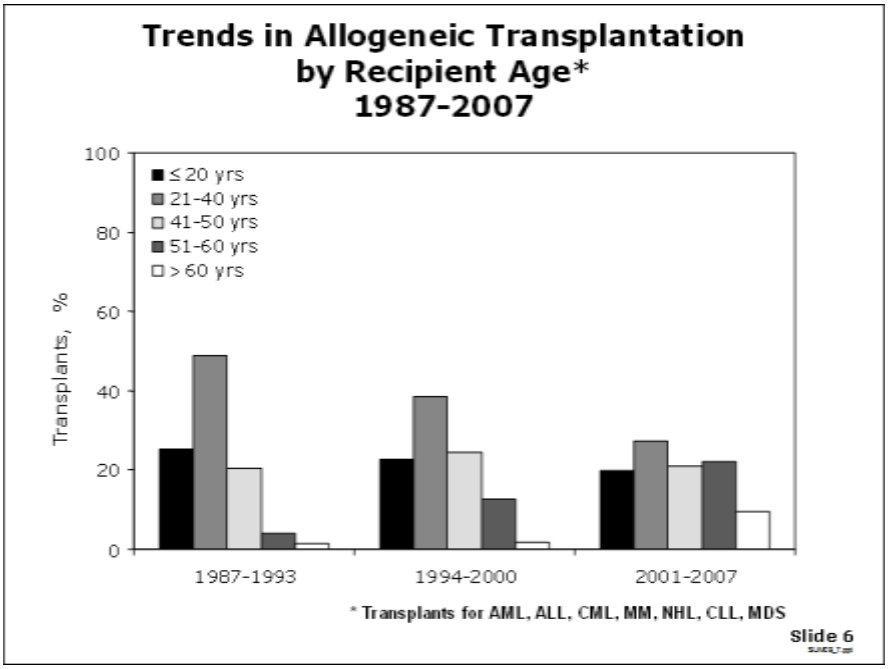
Slide 3: Bone marrow is the primary graft source for transplantation in children, though the use of peripheral blood and umbilical cord blood grafts is increasing. During the period 2003 to 2007, peripheral blood grafts accounted for 28%, and cord blood accounted for 20% of allotransplants in patients younger than 20 years of age. Among adults older than 20 years, peripheral blood is the most common source of allogeneic grafts.



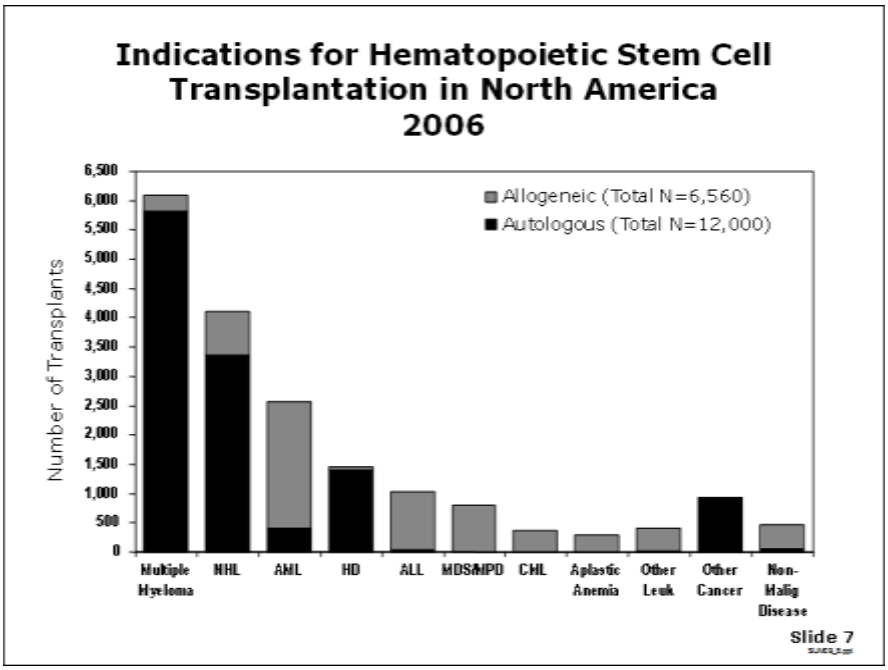
Slide 4: Mobilized peripheral blood progenitor cells are currently the main graft source for autologous HCT, accounting for greater than 90% of transplants in children. The practice of combining bone marrow with peripheral blood stem cells in patients unable to mobilize optimal cell doses has decreased in both adults and children (1%). Better mobilization regimens and patient selection may account for this trend.



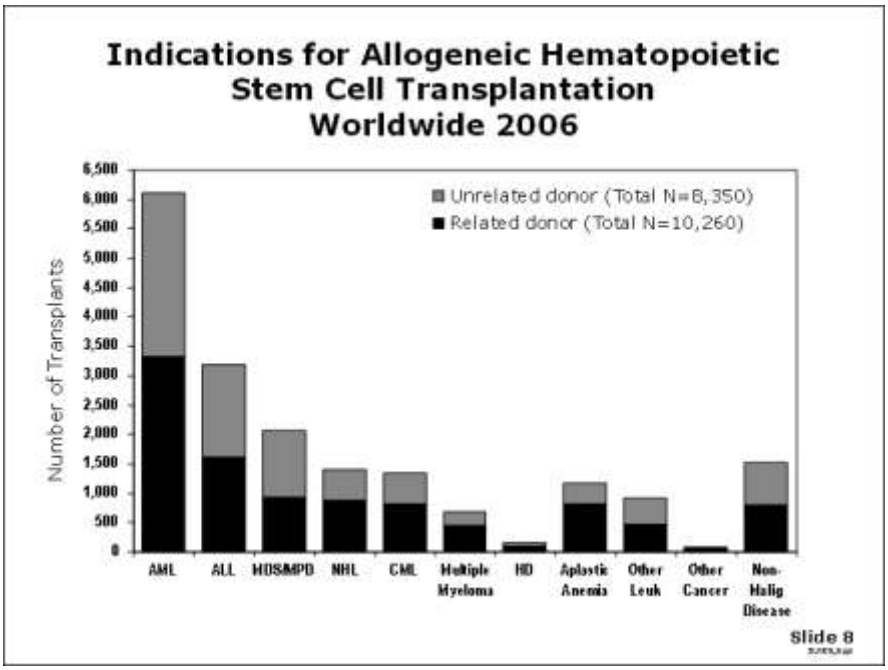
Slide 5



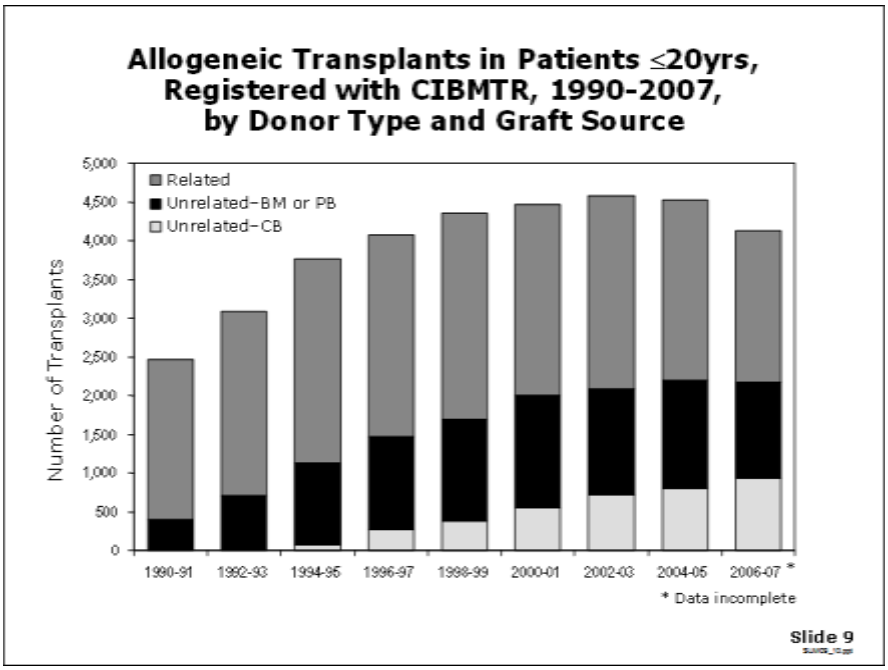
Slides 5 & 6: The numbers of autologous and allogeneic HCTs for treatment of the most common malignant disease indications in patients older than 60 continue to increase. Thirty-two percent of autologous transplant recipients and 10% of allogeneic transplant recipients in 2003-2007 were older than 60 years of age. The majority of autologous transplant recipients (65%) are older than 50 years in this later period.



Slide 7: The most common disease indications for HCT in North America in 2006 were multiple myeloma and lymphoma, accounting for 63% of all HCTs. Multiple myeloma was the most common indication for autologous transplantation and acute myeloid leukemia was the most common indication for allogeneic transplantation.



Slide 8: Approximately 45% of all allogeneic transplants performed worldwide are from unrelated donors. Use of alternative donors depends on the disease indication, recipient's age, and lack of a related donor. Patients with acute leukemias and myelodysplasias most commonly receive unrelated allogeneic transplants. The proportion of unrelated transplants performed in acute leukemias and myelodysplasia are 47% and 55% respectively.



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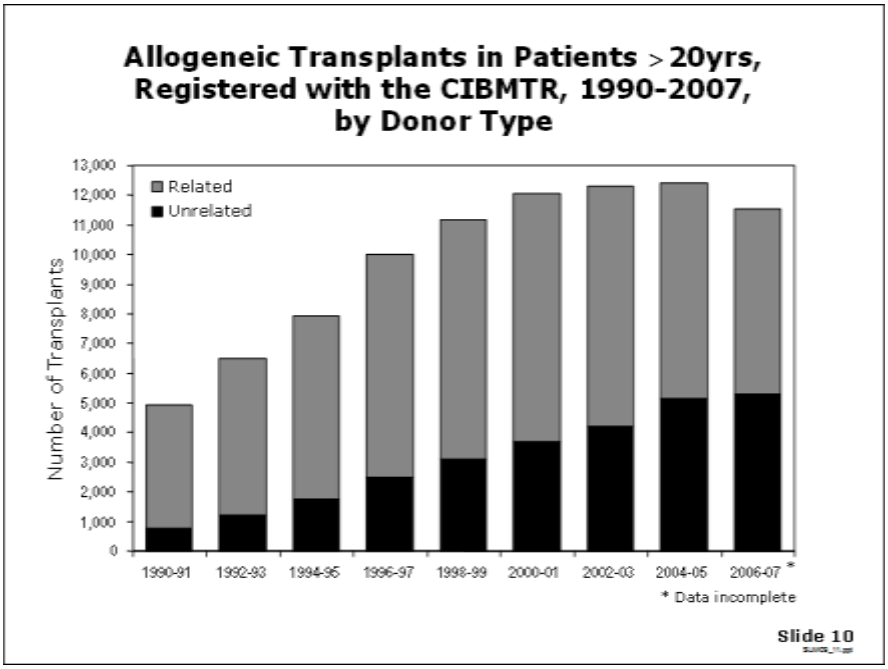
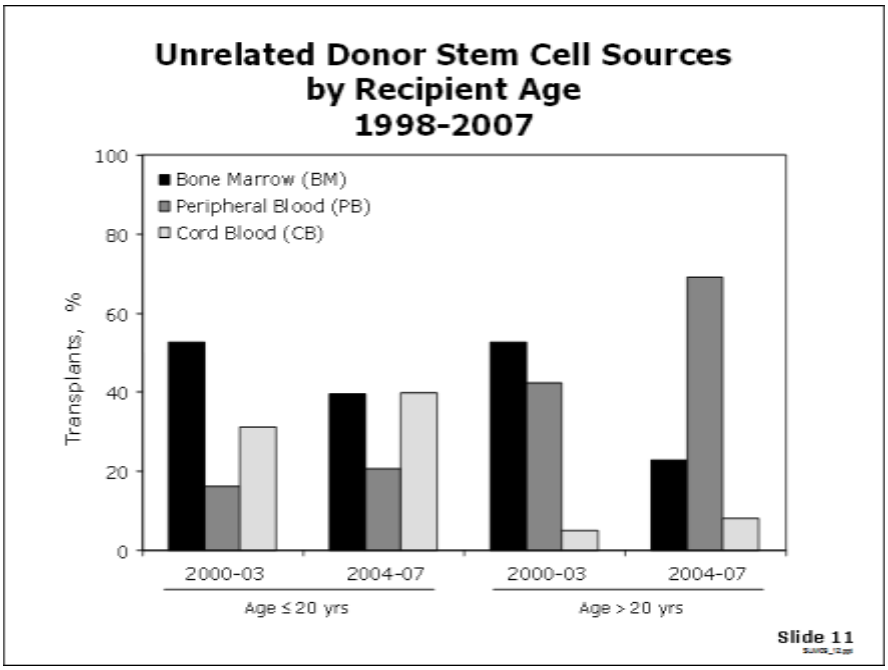
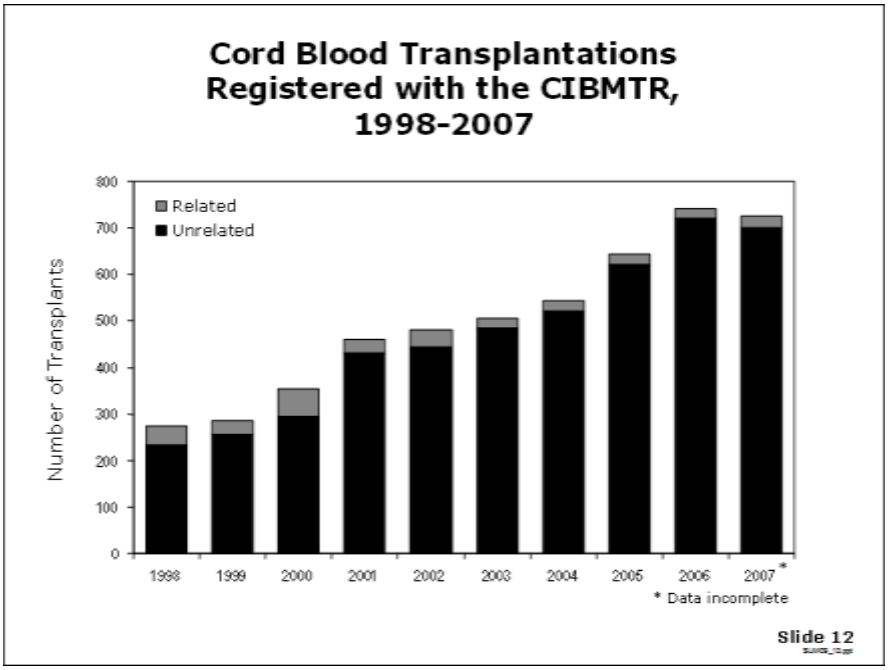


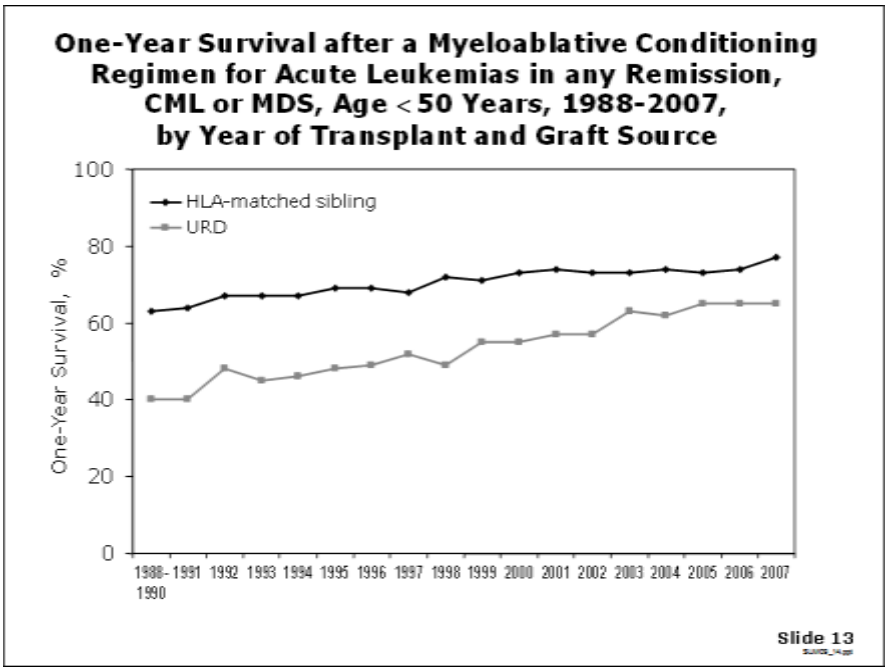
Slides 9 & 10: The proportion of transplants from unrelated donors is steadily increasing for both children and adults. For patients younger than 20, the proportion of unrelated transplants is 53%, with 23% utilizing cord blood as the graft source in 2006-2007. The same general trend is observed in patients older than 20 as well, with 46% of patients receiving unrelated donor transplants. Studies demonstrating similar outcomes between unrelated and related donor transplants, the increased availability of unrelated donors, and the increase in use of cord blood for the pediatric population are all responsible for this increase.



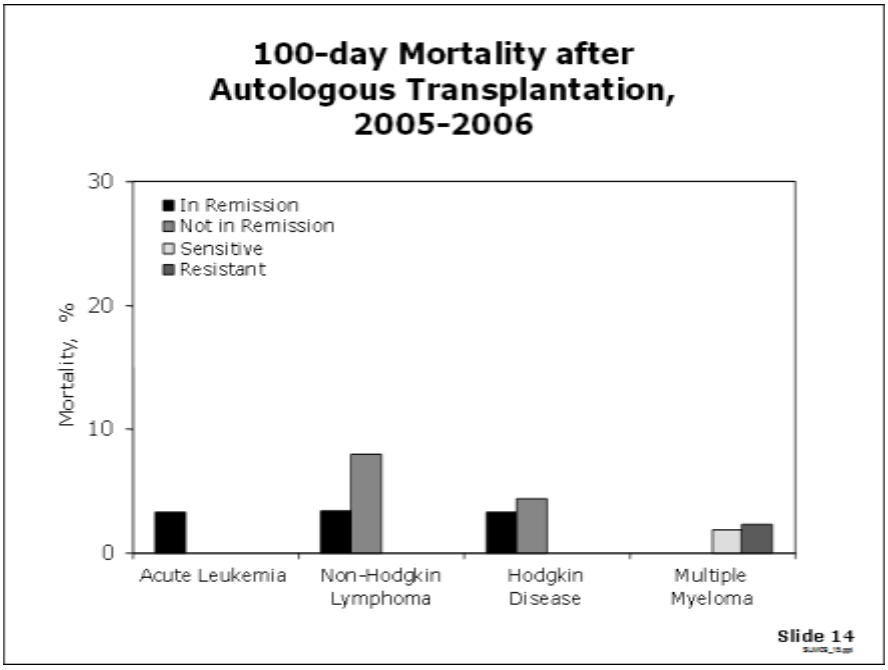
Slide 11: Graft selection for unrelated donor transplantation has shifted from bone marrow to other sources of hematopoietic cells. Among patients younger than 20 years, marrow was used for 40% of unrelated donor transplants in 2004-2007, compared to 53% in 2000-2003. Among patients older than 20 years, marrow accounted for 23% of unrelated donor transplants in 2004-2007, compared to 53% in 2000-2003. The use of cord blood, however, has increased only modestly in patients older than 20 years, reaching just 7%. Limited numbers of cells in single cord blood units is the main barrier for widespread use of this graft source in adults. Similar to related donor allogeneic transplantation, peripheral blood stem cells are the most common graft source for unrelated HCT in adults



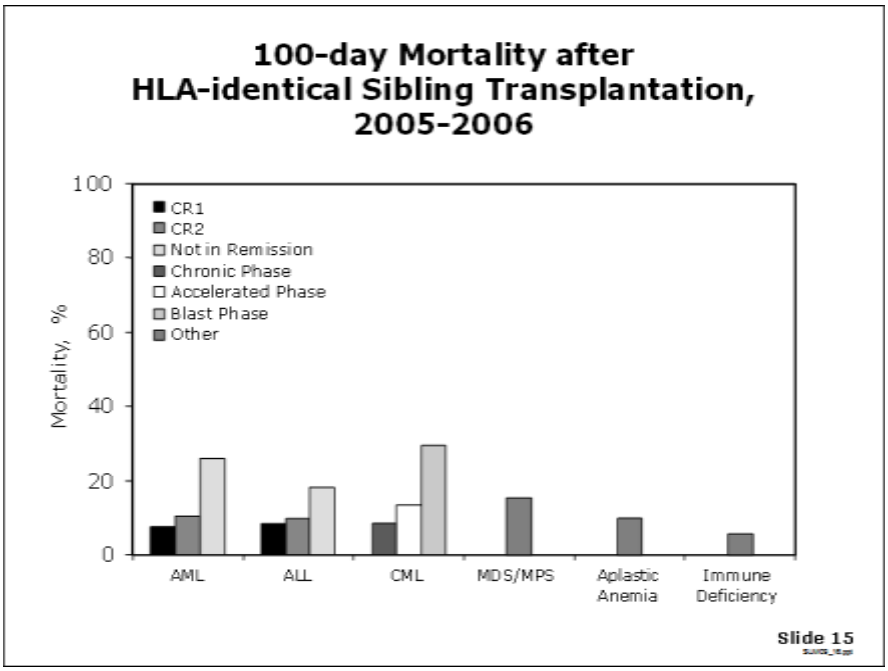
Slide 12: The past 10 years have seen a steady increase in the number of cord blood banks and consequently, in the number of umbilical cord blood transplants. Although cord blood is most frequently an unrelated donor graft source, there are consistent small numbers of related donor cord blood transplants performed every year.



Slides 13: One-year survival rates after transplant have generally improved in the last two decades. Outcomes of unrelated donor transplants are approaching those observed with related donors. Improvements in HLA-matching techniques, with consequently better donor selection, better overall patient selection for transplantation, and improvements in supportive care are the likely explanation for this trend.



Slide 14: The 100-day mortality rate is often cited to reflect the toxicity of the transplantation process. Hundred-day mortality rates are much lower after an autologous than after an allogeneic transplant. The primary disease and disease status at the time of transplantation also significantly affect early post-transplant mortality.



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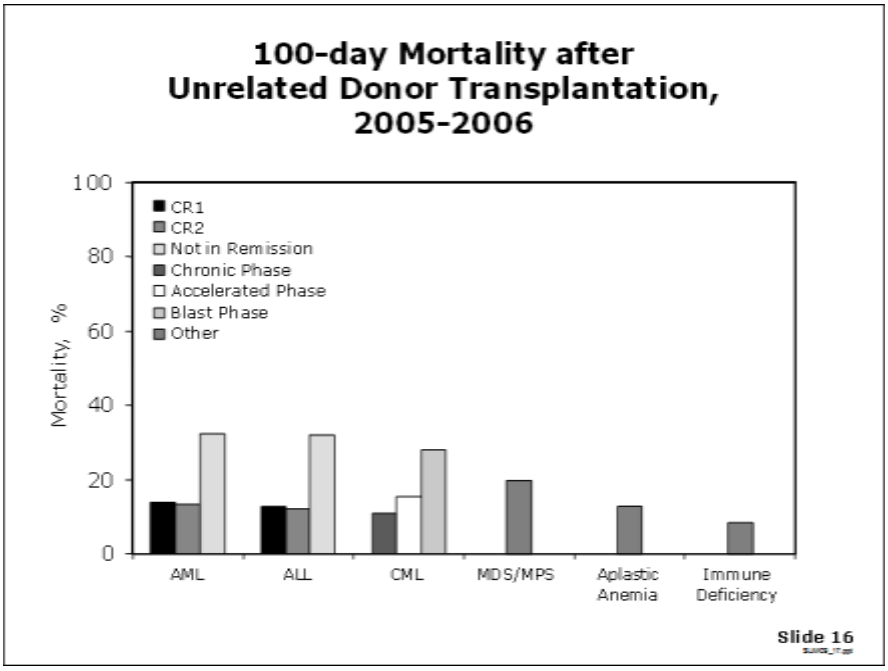

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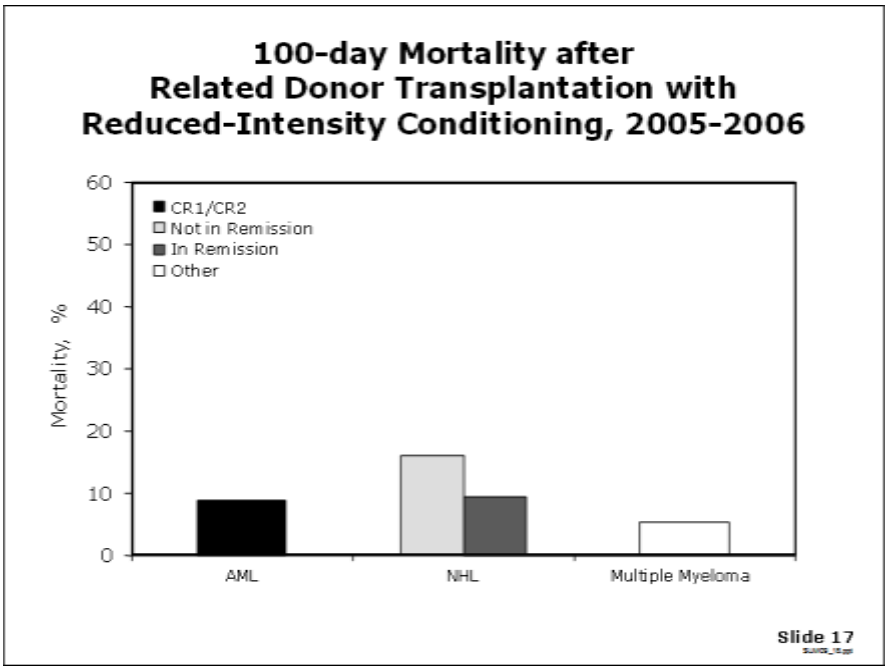
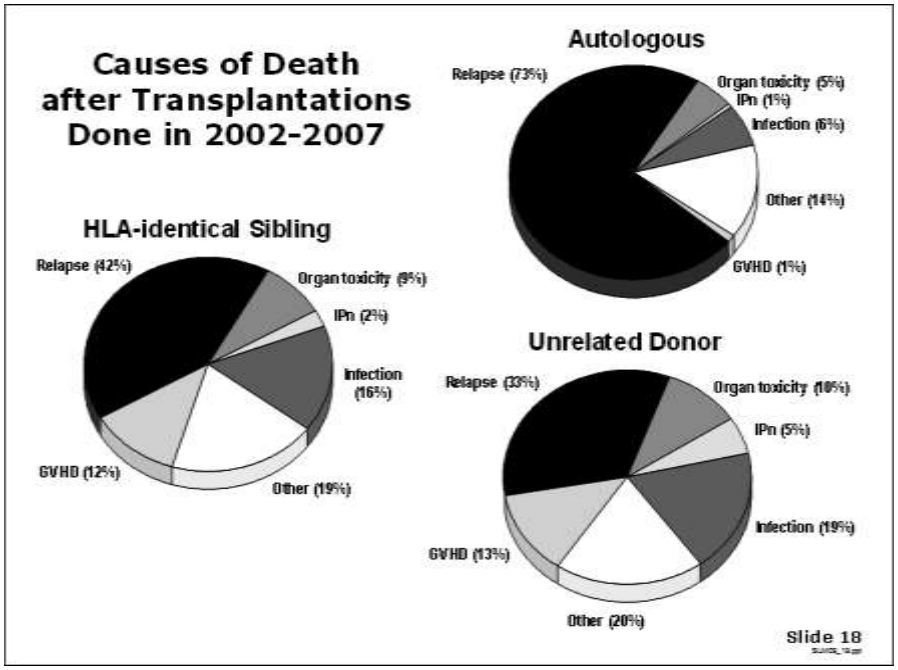
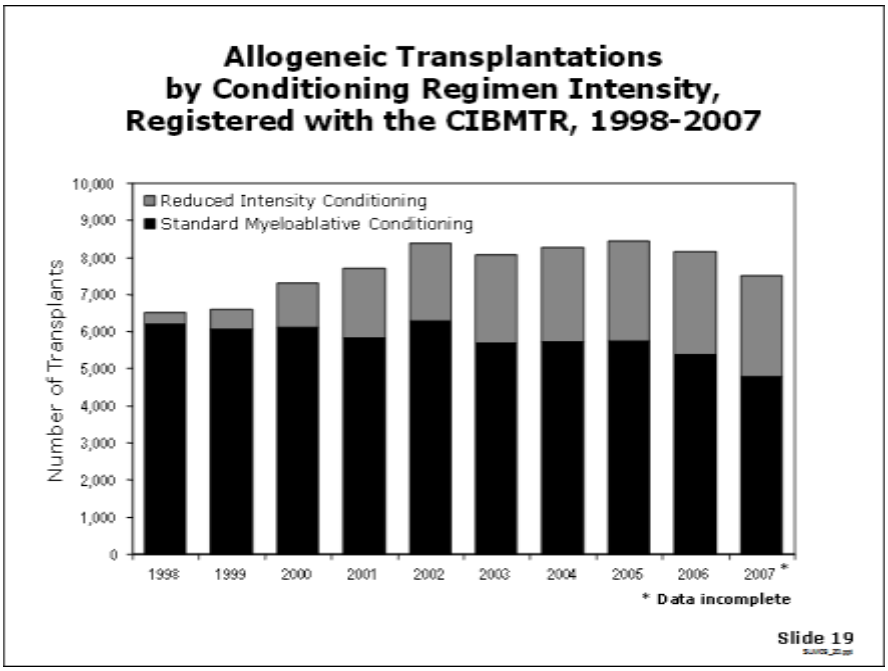


Slides 15 to 17: The effect of disease stage is more apparent for allogeneic transplants. For instance, patients receiving HLA-identical sibling transplants for acute myeloid leukemia in remission have a 100-day mortality rate of 7 to 10% compared to 26% for patients with active leukemia at time of transplantation. Early mortality after an unrelated donor transplant is higher than after an HLA-identical sibling transplant, but this also depends on the disease and disease stage. The causes of death in the first 100 days post-transplant relate mainly to the primary disease, graft-versus-host disease, infection and end-organ damage. Early mortality in patients receiving allogeneic transplants after reduced-intensity conditioning is generally lower. However, patients with active disease have 100-day mortality rates approaching those observed with more intensive conditioning because of high rates of recurrent malignancy.



Slide 18: Relapse is the single most common cause of death after all transplant types, accounting for 73% of deaths after autologous HCT. Graft-versus-host disease (GVHD), interstitial pneumonitis (IPn) and infection are the major causes of death after allogeneic HCT.



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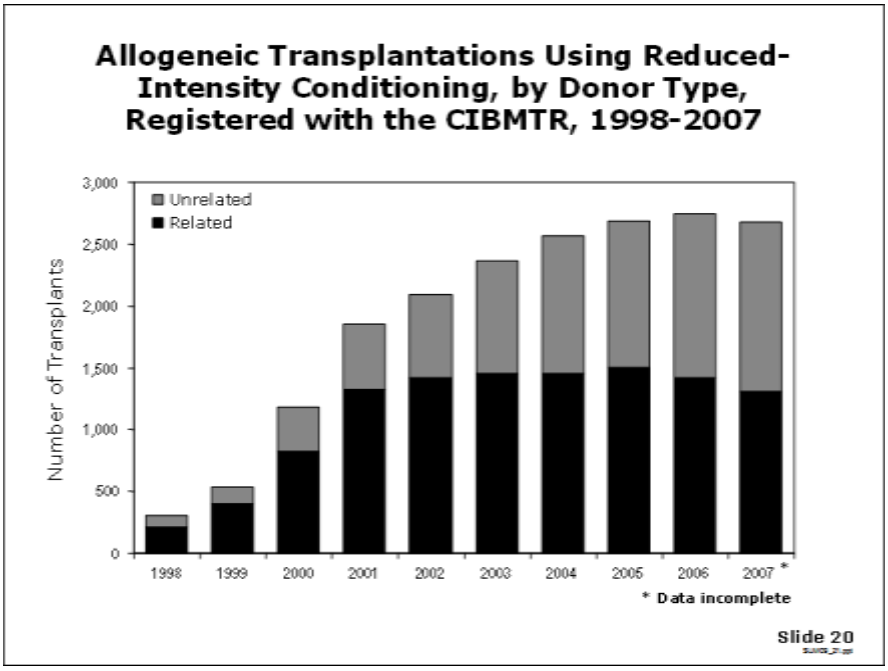
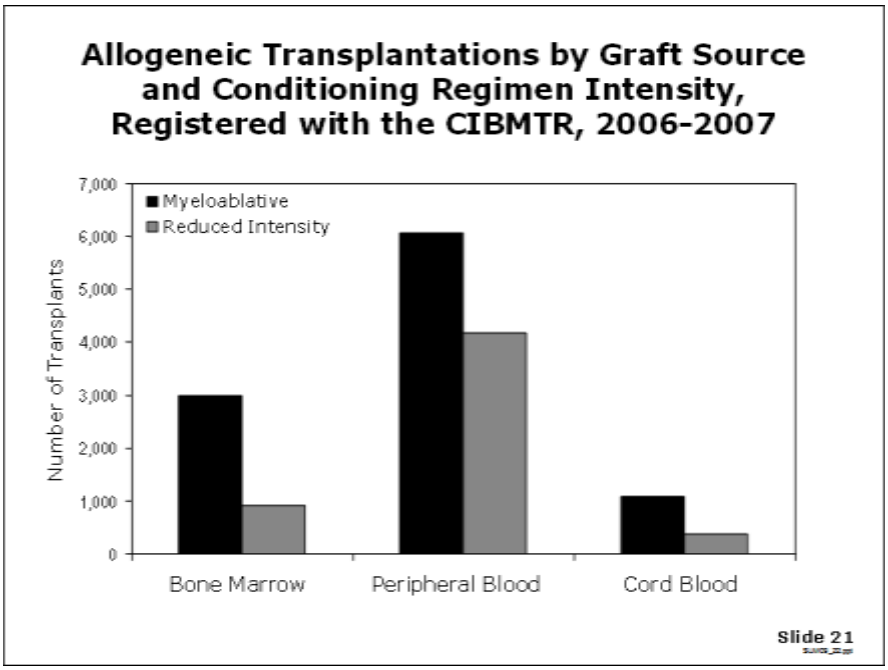


Slide 20



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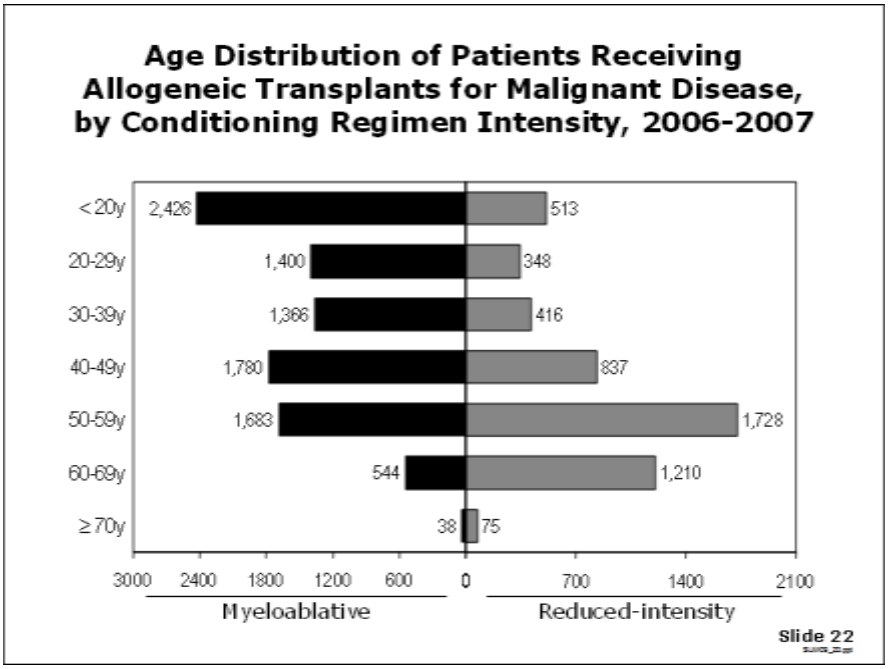
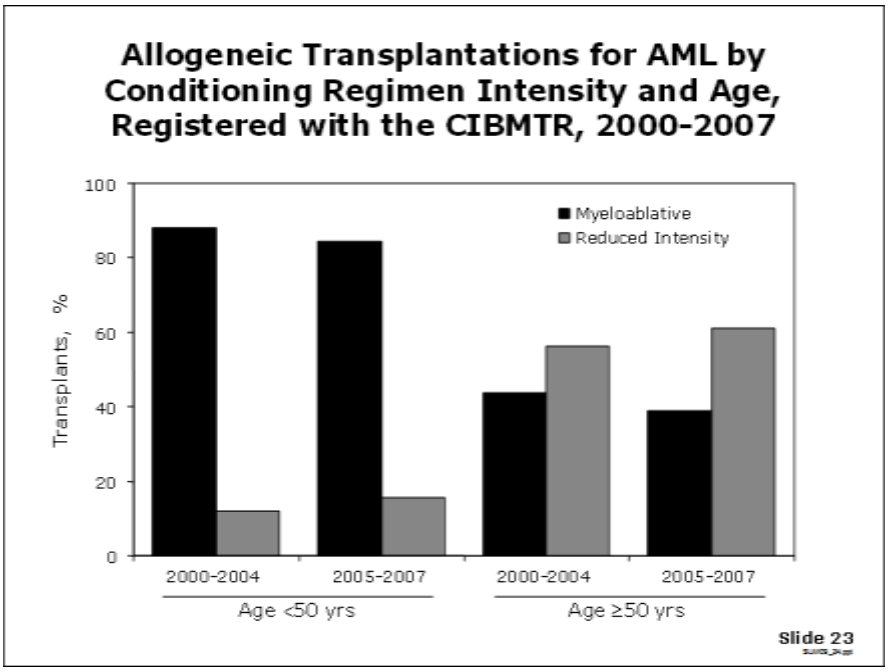


Slides 19 to 22: The numbers of allogeneic transplants performed with reduced-intensity conditioning have steadily increased since 1998, accounting for more than a third of transplants in the later periods. Unrelated donor transplants with reduced-intensity conditioning follow the same trends observed with transplants with myeloablative conditioning, with a slight majority of unrelated over sibling donor transplants. Mobilized peripheral blood is the most common graft source for transplants with reduced-intensity conditioning. The age distribution according to conditioning regimen intensity demonstrates the preferential use of conditioning regimens with lower intensity in patients older than 50 years. Sixty percent of reduced-intensity conditioning recipients are within this age group, compared to fewer than 25% of those receiving standard high-intensity regimens. Patients younger

than 50 years who are ineligible to receive myeloablative conditioning because of co-morbidities may undergo an allogeneic transplant with reduced-intensity conditioning.



Slide 23: Acute myeloid leukemia (AML) is the most common indication for reduced-intensity conditioning allogeneic transplant, and the proportion of these transplants compared to myeloablative regimens is increasing in older patients. Fifty-three percent of patients 50 years and older received an allotransplant with reduced-intensity conditioning in 2005-2007. In younger patients, standard myeloablative intensity regimens remain the most common.