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Authors

Khandelwal, Pooja
Millard, Heather R
Thiel, Elizabeth
[et al.](#)

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Hematopoietic Stem Cell Transplant Activity in Pediatric Cancer between 2008 and 2014 in the United States: A CIBMTR Report

Pooja Khandelwal¹, Heather R Millard², Elizabeth Thiel², Hisham Abdel-Azim³, Allistair A. Abraham⁴, Jeffery J Auletta⁵, Farid Boulad⁶, Valerie I Brown⁷, Bruce M Camitta⁸, Ka Wah Chan⁹, Sonali Chaudhury¹⁰, Morton J Cowan¹¹, Miguel Angel-Diaz¹², Shahinaz M Gadalla¹³, Robert Peter Gale¹⁴, Gregory Hale¹⁵, Kimberly A Kasow¹⁶, Amy K Keating¹⁷, Carrie L Kitko¹⁸, Margaret L MacMillan¹⁹, Richard F Olsson^{20,21}, Kristin M Page²², Adriana Seber²³, Angela R Smith¹⁹, Anne B Warwick²⁴, Baldeep Wirk²⁵, and Parinda A Mehta¹

¹Division of Bone Marrow Transplantation and Immune Deficiency, Cincinnati Children's Hospital Medical Center, Cincinnati, OH

²CIBMTR (Center for International Blood and Marrow Transplant Research), Department of Medicine, Medical College of Wisconsin, Milwaukee, WI

³Division of Hematology, Oncology and Blood & Marrow Transplantation, Children's Hospital Los Angeles, University of Southern California Keck School of Medicine, Los Angeles, CA

⁴Division of Blood and Marrow Transplantation, Center for Cancer and Blood Disorders, Children's National Medical Center, Washington, DC

⁵Host Defense Program, Divisions of Hematology/Oncology/Bone Marrow Transplant and Infectious Diseases, Nationwide Children's Hospital, Columbus, OH

⁶Department of Pediatrics, Memorial Sloan Kettering Cancer Center, New York, NY

⁷Division of Pediatric Oncology/Hematology, Department of Pediatrics, Penn State Hershey Children's Hospital and College of Medicine, Hershey, PA

⁸Midwest Center for Cancer and Blood Disorders, Medical College of Wisconsin and Children's Hospital of Wisconsin, Milwaukee, WI

⁹Department of Pediatrics, Texas Transplant Institute, San Antonio, TX

¹⁰Division of Pediatric Hematology, Oncology and Stem Cell Transplant, Department of Pediatrics, Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL

¹¹Benioff Children's Hospital, San Francisco, CA

¹²Department of Hematology/Oncology, Hospital Infantil Universitario Nino Jesus, Madrid, Spain

¹³Division of Cancer Epidemiology & Genetics, NIH-NCI Clinical Genetics Branch, Rockville, MD

Corresponding author: Elizabeth Thiel, MD, MS, 4476 North Prospect Avenue, Shorewood, WI 53211, Phone: 262-257-3812, Fax: 414-805-0714, elizabeth.thiel@froedtert.com.

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¹⁴Hematology Research Centre, Division of Experimental Medicine, Department of Medicine, Imperial College London, London, United Kingdom

¹⁵Department of Hematology/Oncology, Johns Hopkins All Children's Hospital, St. Petersburg, FL

¹⁶Division of Hematology-Oncology, Department of Pediatrics, University of North Carolina at Chapel Hill, Chapel Hill, NC

¹⁷University of Colorado Children's Hospital, Aurora, CO

¹⁸Vanderbilt University Medical Center, Nashville, TN

¹⁹University of Minnesota Blood and Marrow Transplant Program, Minneapolis, MN

²⁰Division of Therapeutic Immunology, Department of Laboratory Medicine, Karolinska Institute, Stockholm, Sweden

²¹Centre for Clinical Research Sormland, Uppsala University, Uppsala, Sweden

²²Division of Pediatric Blood and Marrow Transplantation, Duke University Medical Center, Durham, NC

²³Hospital Samaritano, Sao Paulo, Brazil

²⁴Department of Pediatrics, Uniformed Services University of the Health Sciences, Bethesda, MD

²⁵Division of Bone Marrow Transplant, Seattle Cancer Care Alliance, Seattle, WA

Abstract

This CIBMTR report describes the use of hematopoietic stem cell transplantation (HSCT) in 4408 pediatric patients with cancer undergoing allogeneic (allo) and 3076 undergoing autologous (auto) HSCT in the United States between 2008 and 2014. In both settings, there was a greater proportion of males (n=4327; 57%), children <10 years of age (n=4412; 59%), Caucasians (n=5787; 77%) and children with a performance score ≥ 90% at HSCT (n=6187; 83%). Leukemia was the most common indication for an allo-transplant (n=4170; 94%), and among these, acute lymphoblastic leukemia (ALL) in second complete remission (n=829; 20%) and acute myeloid leukemia in first complete remission (n=800; 19%) were the most common. The most frequently used donor relation, stem cell sources and HLA match were unrelated donor (n=2933; 67%), bone marrow (n=2378; 54%), matched at 8 out of 8 HLA antigens (n=1098; 37%) respectively. Most allo-transplants used myeloablative conditioning (n=4070; 92%) and calcineurin inhibitors and methotrexate (n=2245; 51%) for acute graft versus host disease prophylaxis. Neuroblastoma was the most common primary neoplasm for an auto-transplant (n=1338; 44%). Tandem auto-transplants for neuroblastoma declined after 2012 (40% in 2011, 25% in 2012, 8% in 2014) whereas tandem auto-transplants have increased for brain tumors (57% in 2008, 77% in 2014). Allo-transplants from relatives other than HLA-identical siblings doubled between 2008 and 2014 (3% in 2008 and 6% in 2014). These trends will be monitored in future reports of transplant practices in the US.

Keywords

Hematopoietic stem cell transplantation; Pediatric cancers

Introduction

Hematopoietic stem cell transplant (HSCT) is an established and widely accepted treatment for a variety of malignant and non-malignant disorders.¹ Indications and approaches to pediatric HSCT differ significantly from adults in several aspects including underlying diagnoses, associated co-morbidities and stem cell sources. HSCT trends over time, in both adult and pediatric patients have been reported by different groups but a focused view on dedicated pediatric- specific HSCT trends is lacking.²⁻⁴

Information on transplant activity is important and relevant for patients, donors, physicians, healthcare providers and regulatory authorities. Establishing the overall trend and activity of HSCT within the pediatric population may lead to improved understanding of the prevalent clinical practices, serve to identify areas of health care and resource disparities and lead to future prospective studies. Lastly, these may also help to predict future trends within the field and help allocate resources to improve patient outcomes.³

This report describes the activity in pediatric HSCT for cancers in the United States between 2008-2014 using data from the Center for International Blood and Marrow Transplant Research (CIBMTR).

Methods

The data reported here comprises all first HSCTs performed in the United States between 2008 and 2014 in children 18 years of age, as reported to the CIBMTR. The CIBMTR is a voluntary working group of greater than 500 transplant centers worldwide that contribute detailed data on consecutive HSCTs to the Statistical Center located at the Medical College of Wisconsin in Milwaukee and at the National Marrow Donor Program (NMDP) Coordinating Center in Minneapolis. Data quality is ensured by on-site audits of participating centers. All studies conducted by the CIBMTR are performed in compliance with all applicable federal regulations pertaining to the protection of human research participants.

With the establishment of the Stem Cell Transplant Outcome Database (SCTOD) in 2007, all allogeneic transplants (allo-HSCT) performed in the United States are required to be registered with the CIBMTR. Reporting for autologous HSCTs to CIBMTR however, is voluntary.

The data reported here summarizes HSCT characteristics based on patient age, diagnosis, type of transplant (autologous versus allogeneic), type of donor (related versus unrelated), intensity of conditioning regimen, Human Leukocyte Antigen (HLA) match (matched versus mismatched) and prevalent graft-versus-host disease (GVHD) prophylaxis.

Disease status for pediatric acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML) were assigned as first (CR1), second (CR2), or third (CR3) complete remission. Tandem transplants within the autologous HSCT (auto-HSCT) group were defined as planned multiple auto-HSCTs in the same patient.

The definition of myeloablative, reduced intensity and non-myeloablative conditioning regimens were based on intent of the conditioning regimen as reported by the treating center to the CIBMTR. Since the intensity of conditioning regimens were determined by the treating physicians and not by the CIBMTR, no clear definitions of the intensity of conditioning regimens can be outlined on this study, but it is assumed that the commonly accepted guidelines were followed.^{5,6}

Results

Allogeneic HSCT

Data on 4408 pediatric allo-HSCT patients from 119 centers are described (Table 1). Median age of patients at the time of HSCT was 10 years (range <1-18) and approximately 3% of patients (n=119) were under 1 year of age. Fifty eight percent (n=2542) of all patients comprised of males. Fourteen percent of patients (n=621) were assigned a performance score < 90 at the time of transplant. Seventy-seven percent (n= 3422) of patients were Caucasians. Fifty-four percent (n=2378) of patients received bone marrow, 28% (n=1247) received umbilical cord blood (UCB) and 18% (n= 783) received peripheral blood stem cells (PBSC) as their stem cell source. Within the UCB group, 28% of patients (n=349) received a double UCB transplant. Sixty seven percent of donors were unrelated (n=2933) while 33 % (n=1475) were related donors.

Forty one percent (n=1207) of unrelated donors received umbilical cord blood and of these patients, 47% (n=570) were HLA matched at 5 of 6 antigens, followed by 29% (n=352), who were HLA matched at <5/6 antigens. Of the patients who received either unrelated bone marrow or peripheral blood stem cells, 37% (n=1098) were HLA matched at 8 out of 8 antigens, followed by 17% (n=493) who were HLA mismatched. In the related donor transplant group, 21% (n=323) were reported as other relative donors. Of these other relative donors, 71% (n=230) were HLA mismatched while 28% (n=90) were HLA matched at 8 of 8 antigens. Seventy nine percent (n=1152) of related donors were HLA identical sibling donors.

Ninety-two percent of patients (n=4070) received a myeloablative conditioning (MAC) regimen, of which 67 % (n=2725) included total body irradiation (TBI). A combination of a calcineurin inhibitor with methotrexate (51%, n=2245) was the predominant GVHD prophylaxis regimen followed by calcineurin inhibitor with mycophenolate mofetil (31%, n=1377). Post-transplant cyclophosphamide as acute GVHD prophylaxis was used in <1% of allo-HSCTs. *Ex-vivo* T-cell depletion (n=122) and CD34+ selection (n=146) was performed in a total of 6% of patients.

The utilization of different intensities of conditioning regimens, donor type/relation and stem cell sources from 2008-2014 are shown in Figure 1A, 1B and 1C. The overall predominance of myeloablative conditioning regimens (~90%) and unrelated donors (~40%) have remained fairly stable over the last 7 years. There was a modest decline in the use of umbilical cord blood (32% in 2008 and 23% in 2014) while the use of bone marrow as a stem cell source has remained relatively stable (50% in 2008 and 58% in 2014). The use of double umbilical cord blood has also remained stable over the last 7 years (25% in 2008 and

23% in 2014). Within donor relation, despite small numbers, it was observed that other relative donors have doubled (3% in 2008 and 6% in 2014) (Figure 1B).

Leukemia—Leukemia was the most common indication for an allo-HSCT (n= 4170, 95%). The number of transplants for various subtypes of leukemia, such as ALL, AML, chronic myeloid leukemia (CML), and bi-phenotypic leukemia have been stable over the past 7 years (Figure 1D). The number of patients transplanted for ALL (n=1896, 46%) was higher than AML (n=1516, 36%) (Table 2). The number of transplants for myelodysplastic syndrome (MDS) and myeloproliferative neoplasms (MPN) have also remained stable over the past 7 years (Figure 1D). TBI was part of the conditioning regimen in 92% (n=1752) of patients with ALL and 35% (n=544) of patients with AML (Table 1).

Within pediatric AML, 98.8% of patients (n=1516) received an allo-HSCT. Of these patients, 29.4% received unrelated UCB (n=447), 27.2% received unrelated bone marrow (n=413) and 21.3% of patients (n=323) received bone marrow from a matched sibling donor (Table 2). Within pediatric ALL, 99.9% of patients received an allo-HSCT. Of these patients, 27.7 % (n=526) received an unrelated UCB, 26% (n=493) received unrelated bone marrow and 24% of patients (n=456) received bone marrow from a matched sibling donor (Table 2). Therefore, within pediatric AML and ALL, the use of an unrelated UCB was comparable to bone marrow from either a sibling or unrelated donor. Unrelated UCB use was also comparable to marrow utilization from either a sibling or unrelated donor in pediatric bi-phenotypic leukemia, and MDS/MPN (Table 2).

Trends of disease status prior to transplant for pediatric ALL and AML are shown in Figure 1E and 1F. Transplant in CR1 remains the most common indication in AML (n=800, 52% of all AML transplants) while transplant in CR2 is most common in ALL (n=829, 43.7% ALL transplants) over the last 7 years. Trends for transplant in CR2, CR3, and in relapse remain unchanged over the last 7 years for AML. Similarly, trends for transplant in CR1, primary induction failure, and in relapse remain unchanged in pediatric ALL over the last 7 years. A small decrease in transplants in CR3 in pediatric ALL (16% in 2008 and 11% in 2014) was observed.

Lymphoma—Approximately 5% of all allogeneic HSCTs (n=217) were performed for an underlying diagnosis of a lymphoma. Non-Hodgkin lymphoma (NHL) was the most common indication for an allo- HSCT among these disorders (85%, n=184). Allo-HSCT for Hodgkin lymphoma demonstrated a decline in 2010, followed by an increase in 2011 and then a slow decline again (Figure 1G). Allogeneic HSCT for NHL also demonstrated a decline in 2011 followed by an increase annually thereafter. Similar to pediatric leukemia, unrelated bone marrow (n=46) and unrelated UCB (n=36) were comparable to sibling marrow transplants (n=39) in pediatric allo-HSCTs for NHL (Table 2).

Autologous HSCT

Data on 3076 pediatric auto-HSCT patients from 113 centers are shown in Table 1. Median age of patients at the time of HSCT was 5 years (range<1-18 years) and 70% (n=2159) were between 1-10 years of age. Males comprised 58% (n=1785) of all autologous HSCT patients. Sixteen percent (n=507) of patients reported a performance score of <90 at the time

of transplant. Similar to allo-HSCT, 77% (n=2365) of patients were Caucasian. Of the auto-HSCTs, 23% (n=717) were tandem HSCTs. PBSC were used in 98% (n=3024) of all auto-HSCTs.

Neuroblastoma was the predominant indication for single auto-HSCT (n=1338; 43.4%) followed by medulloblastoma (n=389; 12.6%), with overall percentages remaining stable from 2008 to 2014 (Figure 2A). The use of tandem auto-HSCT for neuroblastoma has declined since 2012 (40% in 2011, 25% in 2012, 8% in 2014) while it has increased for central nervous system tumors from 2008 to 2014 (57% in 2008, 77% in 2014) (Figure 2B). Auto-HSCT activity for Ewing's family of tumors was low and variable over the last 7 years (e.g. 9% of auto-HSCTs in 2008-2009 and 4% in 2013). Lymphoma was the indication for transplant in 16% (n=506) of auto-HSCTs from 2008 to 2014. Within this group, Hodgkin lymphoma was the most common indication (79%, n=401). Auto-HSCT for Hodgkin lymphoma shows increased activity over last seven years (74% in 2008 and 84% in 2014). In contrast, activity in auto-HSCT for NHL shows a decline from 2008 to 2014 (26% in 2008 and 15% in 2014) (Fig 1H).

Discussion

This pediatric focused report from the CIBMTR highlights contemporary trends in allogeneic and autologous HSCT use for pediatric cancers in the United States. Mandatory reporting ensures that data capture by the Stem Cell Therapeutic Outcomes Database (SCTOD) for allo-HSCT is a complete and reliable representation of current practices.

In the US, unrelated donor transplants have surpassed transplants using sibling donors for malignancies. Increase in unrelated donor transplants in the US is likely a testament to an expanding unrelated donor registry, better HLA matching, improved supportive care for HSCT and comparable outcomes of related and matched unrelated donors.⁷ Increasing unrelated donor transplants could also be a reflection of smaller families, which lowers the likelihood of finding a sibling donor. The majority of children undergoing an allogeneic HSCT for cancers were Caucasians. Although this is not surprising given that the majority of the US population is comprised of Caucasians, it could perhaps be a reflection of the limited NMDP donor pool for non-Caucasians and an underlying health care disparity in the minority groups.⁸

Mismatched unrelated donor stem cell sources (<8 out of 8 HLA matched bone marrow or peripheral blood and <6/6 HLA matched umbilical cord blood; n=1415) are being utilized comparably to fully matched unrelated donor stem cell sources (8 of 8 HLA matched bone marrow or peripheral blood stem cells and 6 out of 6 HLA matched cord blood; n=1266). This is likely due to tolerance of HLA mismatched donors in high-risk pediatric malignancies along with improved cord blood banking and supportive care measures for patients. There is also a potential for an improved graft-versus-leukemia effect due to the increased tolerance for HLA mismatch.

Percentage of other relative donors has doubled in 2014 compared to 2008; although the overall numbers of these remain small. The majority of other relative donors were HLA

mismatched. As detailed information regarding the degree of HLA match for this specific subgroup was beyond the scope of this report, it is difficult to comment with certainty if these other relative donors were being utilized for haplo-identical transplants.⁹ The 2013 EBMT survey reports an increasing use of haplo-identical donor transplants in Europe.¹⁰ It is possible that, especially with novel strategies such as post-HSCT cyclophosphamide and TCR $\alpha\beta$ T-cell depletion,¹¹ haplo-identical HSCTs may increase in the United States as well in the future. This trend will need to be observed closely in future reports.

The preference for bone marrow and UCB grafts over PBSCs for allo-HSCT in pediatric setting remain steady, likely due to the known higher risk of chronic GVHD associated with PBSC grafts.¹² Unrelated UCB grafts are still being used comparably to bone marrow grafts in pediatric AML, ALL, bi-phenotypic leukemia and MPN/MDS. This is likely related to increased and improved inventories of the cord blood banks and faster availability of this product, which is an important consideration during HSCT for malignancies. Use of double UCB grafts have remained stable over the last 7 years, however it is possible that its use will decline in subsequent years following the results of the BMT Clinical Trials Network/ Children's Oncology Group study which did not demonstrate any survival advantage after a double UCB transplant in hematological malignancies¹³ as well as the increasing use of stem cell expansion modalities and haplo-identical donor transplants. Ultimately, the overall cost of procuring double cord units and the consideration of improved stem cell doses in double cord blood units in individual instances may continue to influence this parameter and our supposition will need to be evaluated in future observations over years.

Interestingly, within pediatric leukemia, TBI was employed in 35% of AML patients despite lack of evidence of a distinct advantage of using TBI in children with AML in CR1 or beyond.¹⁴⁻¹⁶ We anticipate that in future observations, the use of TBI in AML will decline in the face of existing evidence which demonstrates a lack of superiority of TBI over busulfan based regimens. Transplant trends for pediatric ALL in CR2 and AML in CR1, the two most common indications, remain unchanged over the last 7 years. The stable rates of transplant for children with AML in CR1 during 2008-2014 probably reflects the guidelines in Children's Oncology Group (COG) AAML0531 (2006-2010) and the current COG study AAML1031 (2011- present) where low risk patients with AML in CR1 are treated with chemotherapy and transplant is deferred until CR2. The overall numbers of HSCTs for CML, MDS/MPN/other myeloid disorders, bi-phenotypic leukemia and other leukemia have also remained stable over 2008-2014. A slight decline in transplants for ALL in CR3 is likely explained either by advances in prognostic factors such as minimal residual disease monitoring and referral in CR2 if patients demonstrate MRD positivity despite late relapse¹⁷ or by an increasing use of chimeric-antigen-receptor (CAR)-T cells¹⁸ and/or novel biologic therapies¹⁹ over the past few years.

We recognize that open clinical trials during the time of our data collection might have influenced several observations made in this report. Examples of such trials include the Bone Marrow Transplant – Clinical Trials Network protocol 0501 which was a phase III randomized multi- institutional clinical trial of single versus double umbilical cord blood transplantation in children with hematological malignancies using fludarabine, cyclophosphamide and TBI as the conditioning regimen. The specifications of this trial

could have contributed to the use of TBI in pediatric AML and the completion of this trial in 2012 could account for the decline in UCB use over time in all allogeneic transplants. We believe that it would be prudent to view the results of our study through the lens of ongoing open clinical trials during the time of our data reporting, which could have a significant influence on some of the trends observed.

Within lymphomas, allo-HSCTs for NHL are predominant and stable over the past 7 years. There was an increase in allo-HSCTs for Hodgkin lymphoma in 2011 followed by a slow decline over the next few years. In 2010, a retrospective report demonstrated a survival advantage for patients who receive a RIC allo-HSCT for Hodgkin lymphoma after a relapse following an auto-HSCT²⁰, likely lending enthusiasm to this approach. However, overall number of patients receiving an allo-HSCT for Hodgkin lymphoma remains small, and therefore this trend should be interpreted with caution.

High dose chemotherapy and auto-HSCT is still the standard of care for patients with Hodgkin lymphoma who relapse with non-localized disease after frontline therapy and this is reflected by the predominance of auto-HSCTs for Hodgkin lymphoma within the lymphoma group. Neuroblastoma continues to be the predominant indication for auto-HSCTs over the past 7 years. Tandem transplants for neuroblastoma however demonstrated a decline 2012 onwards. A likely reason for this transient decline in tandem transplants for neuroblastoma could be due to the increased use of immune based therapies such as anti-GD2 antibodies.²¹ This decline will need to be evaluated in future observations, since the most recent randomized controlled trial conducted by the Children's Oncology Group demonstrated an improved event free survival with tandem transplants for neuroblastoma.²² Tandem transplants are increasing for CNS tumors, consistent with data that has shown improved survival with this approach.^{23, 24}

We anticipate that this observed increase in tandem transplants in children with CNS tumors may change in the future with the start of the randomized clinical trial Head Start 4, which will randomize high risk CNS tumor patients to receive either one or three autologous transplants. Transplant for Ewing's sarcoma has remained somewhat controversial with conflicting reports regarding its efficacy. European data and limited retrospective reports demonstrate improved outcomes with auto-HSCT in patients with Ewing sarcoma with high risk features.^{25, 26} No clear trend was observed in our report with regards to auto-HSCT for Ewing's family tumors and this will also require closer and longer term follow up.

This study has several limitations. Despite the presence of the SCTOD, the data capture is dependent on available reporting from treating centers, especially as reporting on autologous HSCT data to the CIBMTR is voluntary. This report focusses on trends reflecting changes in practice and does not include information pertaining to degree of HLA matching for other relative donors, rates of overall and event-free survival and rates of complications such as acute and chronic GVHD. Despite large overall number of patients, several sub-categories including transplants for ALL in CR3, other family donor transplants and allo-HSCT for Hodgkin lymphoma remain small.

In conclusion, while most pediatric activities in HSCT have remained stable over the last 7 years, several important evolving trends have become apparent. We observed a recent decline in tandem transplants for neuroblastoma and an increase in tandem transplants for central nervous system tumors. We speculate that tandem transplants for neuroblastoma might re-emerge in subsequent years in the United States based on recent clinical trial results. We also speculate that tandem transplants may decline for children with CNS tumors during the enrollment of Head Start 4 and the results of this trial may influence this trend in future observations. We see a small decrease in ALL transplants in CR3 and speculate this to be a result of better prognostic markers and novel cellular and biologic therapies that have emerged recently. We also note the minor increase in the use of other family donors, despite very small numbers and will need to follow this trend over time. Most current publications related to increasing haplo-identical transplants, and decline in the use of double cord blood transplants will likely change this landscape and should be monitored closely in future reports. Similarly, we expect further paradigm changes in the overall HSCT trends for cancer especially with increasing use of cellular therapy and targeted immunotherapies for solid tumors.

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Highlights

- In patients with leukemia, acute lymphoblastic leukemia in second complete remission was the most common indication for allogeneic transplantation
- Neuroblastoma was the predominant indication for single autologous transplant
- Use of tandem autologous transplants has increased for central nervous system tumors while it has declined for neuroblastoma

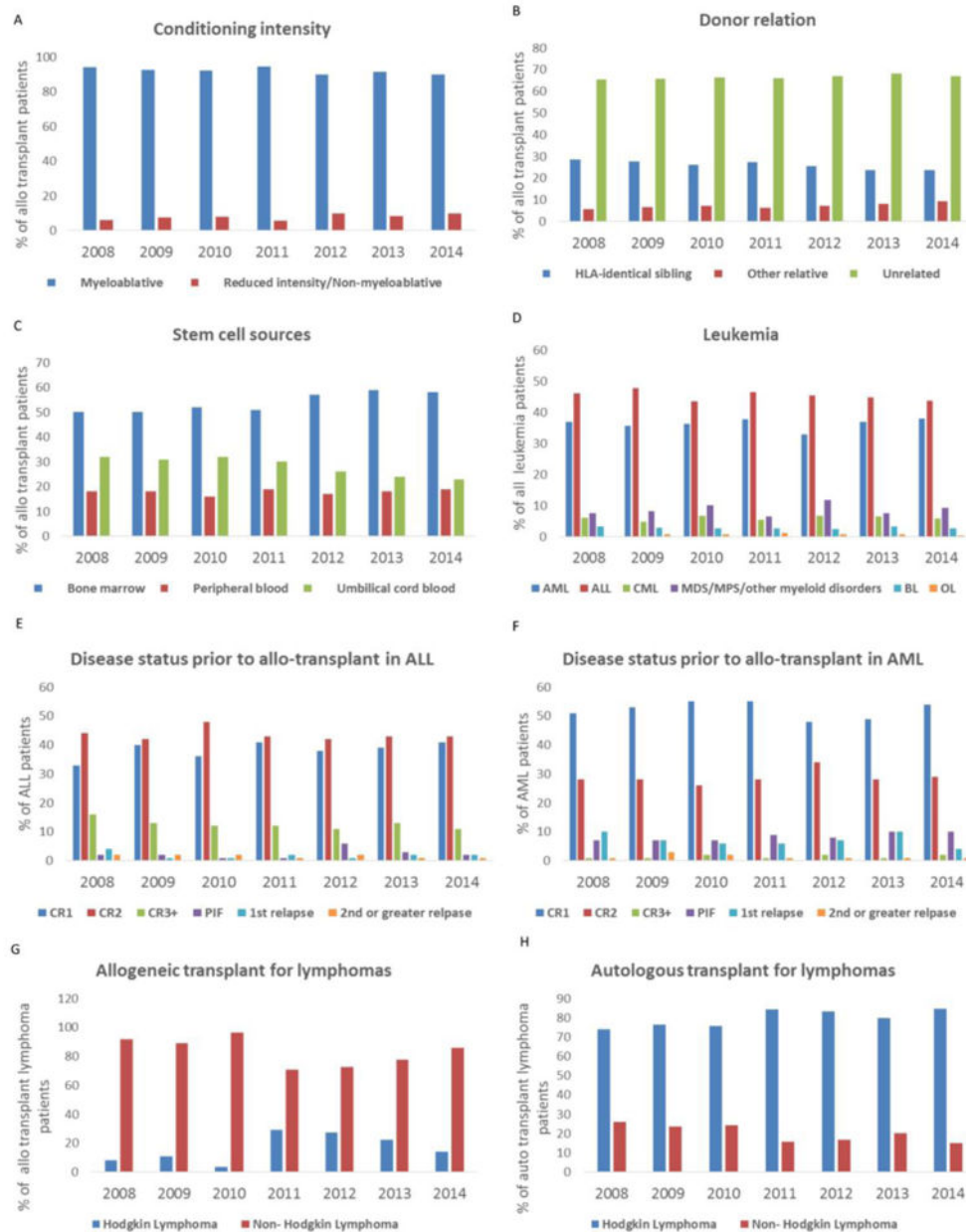


Figure 1.

1A. Conditioning intensity for all allogeneic transplants between 2008 and 2014. The percentage of allogeneic transplant patients who received either myeloablative or a reduced intensity or non/myeloablative conditioning regimen are shown.

1B. Donor relation in allogeneic HSCT between 2008 and 2014. The percentage of all allogeneic transplants that received either an HLA-identical sibling donors, other relative donors or unrelated donors are shown.

1C. Stem cell sources in allogeneic HSCT between 2008 and 2014. The percentage of all allogeneic transplants that received either a bone marrow, peripheral blood stem cell or umbilical cord blood are shown.

1D. Allogeneic transplant for various leukemia subtypes between 2008 and 2014. The percentage of all leukemia patients that received an allogeneic transplant that were acute myeloid leukemia (AML), acute lymphoid leukemia (ALL), chronic myeloid leukemia (CML), myelodysplastic syndrome/myeloproliferative neoplasms or other myeloid disorders (MDS/MPN), bi-phenotypic leukemia (BL) or other leukemia (OL) are shown.

1E. Disease status prior to an allogeneic transplant in acute lymphoid leukemia (ALL) is shown. Percentage of ALL patients transplanted in first complete remission (CR1), second complete remission (CR2), third complete remission (CR3), primary induction failure (PIF), first relapse and second or greater relapse is shown.

1F. Disease status prior to an allogeneic transplant in acute myeloid leukemia (AML) is shown. Percentage of AML patients transplanted in first complete remission (CR1), second complete remission (CR2), third complete remission (CR3), primary induction failure (PIF), first relapse and second or greater relapse is shown

1G. Percentage of patients with lymphoma who received an allogeneic transplant between 2008 and 2014.

1H. Percentage of patients with lymphoma who received an autologous transplant between 2008 and 2014.

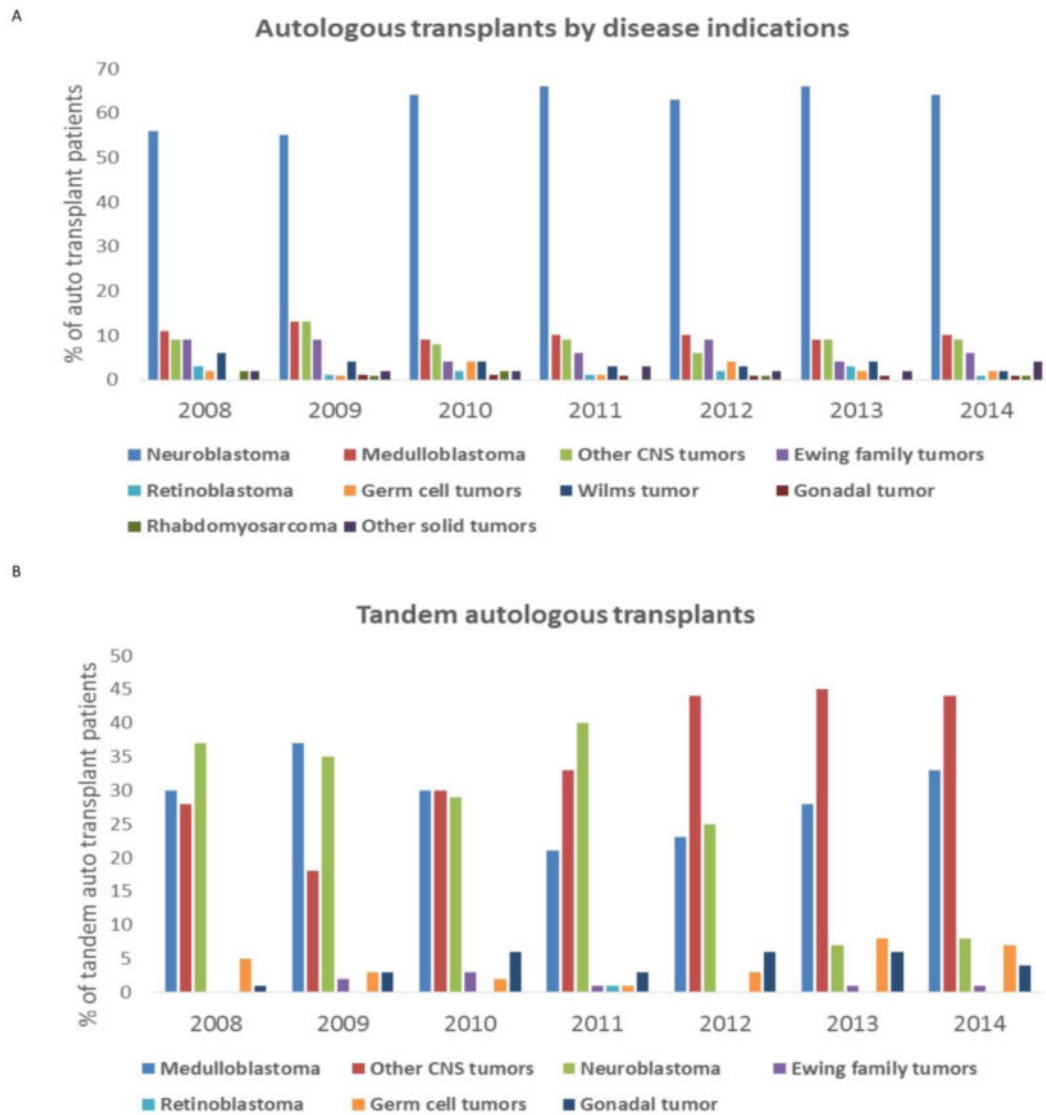


Figure 2.

2A. Percentage of patients with various solid tumors who underwent an autologous transplant between 2008 and 2014. Percentage of all autologous transplant patients with an underlying diagnosis of a neuroblastoma, medulloblastoma, other central nervous system (CNS) tumors, Ewing family tumors, retinoblastoma, germ cell tumors, Wilms tumor, gonadal tumors, rhabdomyosarcoma and other solid tumors.

2B. Percentage of patients with various solid tumors who received tandem autologous HSCTs between 2008 and 2014. Percentage of all tandem autologous transplant patients with an underlying diagnosis of medulloblastoma, other central nervous system (CNS) tumors, neuroblastoma, Ewing family tumors, retinoblastoma, germ cell tumors and gonadal tumors.

Table 1

Demographics and transplant characteristics in pediatric patients undergoing allogeneic and autologous transplant between 2008 and 2014.

	Allogeneic HSCT N (%)	Autologous HSCT N (%)
Number of patients	4408	3076
Number of centers	119	113
Median age at transplant (range), years	10 (<1-18)	5 (<1-18)
< 1 year	119 (3)	84 (3)
1-10 years	2253 (51)	2159 (70)
11-18 years	2036 (46)	833 (27)
Gender		
Male	2542 (58)	1785 (58)
Female	1866 (42)	1291 (42)
Lansky performance score at transplant		
90	3722 (84)	2465 (80)
<90	621 (14)	507 (16)
Missing	65 (1)	104 (3)
Race		
Caucasian/White	3422 (78)	2365 (77)
Black	471 (11)	428 (14)
Asian/Hawaiian/Pacific Islander	252 (6)	144 (5)
Native American/American Indian	43 (<1)	16 (<1)
Unknown/Declined	220 (5)	123 (4)
Ethnicity		
Hispanic	1169 (27)	563 (18)
Non- Hispanic	3180 (72)	2446 (80)
Missing	59 (1)	67 (2)
Treatment protocol		
Single Allogeneic	4390 (99)	N/A
Tandem Autologous-Allogeneic	18 (<1)	N/A
Single Autologous	N/A	2359 (77)
Tandem Autologous-Autologous	N/A	717 (23)
Stem cell source		
Bone marrow	2378 (54)	49 (2)
Peripheral blood	783 (18)	3024 (98)
Umbilical cord blood	1247 (28)	3 (<1)
Donor (allogeneic HSCT only)		
HLA-identical sibling [^]	1152 (26) [^]	N/A
Other relative	323 (7)	

	Allogeneic HSCT N (%)	Autologous HSCT N (%)
Unrelated donor	2933 (67)	
HLA Match (other relative donor)		
Matched	90 (28)	
Mismatched	230 (71)	
Unknown	3(1)	
HLA Match (unrelated donor)		
Peripheral blood or bone marrow matched 8/8	1098 (37)	
Peripheral blood or bone marrow mismatched (<8/8)	493 (17)	
Peripheral blood or bone marrow matching unknown	135 (5)	
Umbilical cord blood match matched (6/6)	168 (5)	
Umbilical cord blood mismatched (5/6)	570 (20)	
Umbilical cord blood mismatched (<5/6)	352 (12)	
Missing umbilical cord data	117 (4)	
Conditioning intensity (as reported by center, allogeneic HSCT only)		
Myeloablative	4070 (92)	N/A
Reduced intensity/Non-myeloablative	302 (7)	
Missing	36 (<1)	
Total body irradiation containing conditioning		
No	1350 (31)	2511 (82)
Yes	2725 (62)	23 (<1)
Missing	333 (8)	542 (18)
Total body irradiation in acute lymphoid leukemia		
No	117 (6)	
Yes	1752 (92)	
Missing	28 (2)	
Total body irradiation in acute myeloid leukemia		
No	796 (52)	
Yes	544 (35)	
Missing	193 (13)	
GVHD prophylaxis (allogeneic HSCT only)		
Ex-vivo T-cell depletion	122 (3)	N/A
CD34+ selection	146 (3)	
Post-transplant Cyclophosphamide	28 (<1)	
Calcineurin inhibitor alone (either tacrolimus or cyclosporine)	178 (4)	
Calcineurin inhibitor + Mycophenolate mofetil	1377 (31)	
Calcineurin inhibitor + Methotrexate	2245 (51)	
Calcineurin inhibitor + other	234 (5)	
Other(s) *	52 (1)	
Missing	26 (<1)	

	Allogeneic HSCT N (%)	Autologous HSCT N (%)
Median follow-up of survivors (range), months	37 (<1-88)	35 (1-84)

[^] Syngeneic HSCTs n=9

^{*} MTX ± other (not CNI) (n=43), MMF ± other (not CNI) (n=9)

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Table 2

Pediatric allogeneic and autologous transplants described by donor and stem cell source.

Indication for transplant	Allogeneic (Allo)										Autologous (Auto)						Total		
	Related Donors					Unrelated Donors					BM	PB	CB	Allo	Auto	Total Allo + Auto			
	HLA id sibling		Other relative			Total	BM	PB	CB	Total							BM	PB	CB
	BM*	PB^	CB#	BM	PB														
Total	957	165	30	185	128	10	1475	1236	490	1207	2933	49	3024	3	4408	3076	7484		
Leukemia	910	135	29	168	117	10	1369	1177	455	1169	2801	2	16	0	4170	18	4188		
AML&	323	46	11	56	39	3	478	413	178	447	1038	2	15	0	1516	17	1533		
ALL@	456	57	15	85	58	3	674	493	203	526	1222	0	1	0	1896	1	1897		
CML †	45	10	2	8	2	1	68	97	20	65	182	0	0	0	250	0	250		
Bi-phenotypic leukemia	25	8	0	7	8	0	48	25	8	37	70	0	0	0	118	0	118		
MPN %MDS\$	56	13	1	12	8	3	93	139	45	86	270	0	0	0	363	0	363		
Other leukemias	5	1	0	0	2	0	8	10	1	8	19	0	0	0	27	0	27		
Lymphoma	44	25	1	13	9	0	92	57	32	36	125	11	495	0	217	506	723		
Hodgkin lymphoma	5	5	0	4	2	0	16	11	6	0	17	5	396	0	33	401	434		
Non-Hodgkin lymphoma	39	20	1	9	7	0	76	46	26	36	108	6	99	0	184	105	289		
Plasma cell disorder	0	1	0	0	0	0	1	1	0	0	1	0	5	0	2	5	7		
Solid tumors	3	4	0	4	2	0	13	1	3	2	6	36	2508	3	19	2547	2566		
Medulloblastoma	1	0	0	0	0	0	1	1	0	0	1	11	377	1	2	389	391		
Other CNS tumors	0	0	0	0	0	0	0	0	0	0	0	13	395	1	0	409	409		
Neuroblastoma	1	2	0	1	0	0	4	0	0	1	1	4	1333	1	5	1338	1343		
Ewing family tumors	1	1	0	0	2	0	4	0	2	1	3	2	127	0	7	129	136		
Retinoblastoma	0	0	0	0	0	0	0	0	0	0	0	3	32	0	0	35	35		
Germ cell tumors	0	0	0	0	0	0	0	0	0	0	0	0	68	0	0	68	68		
Wilms tumor	0	0	0	0	0	0	0	0	0	0	0	2	68	0	0	70	70		
Gonadal tumors	0	0	0	0	0	0	0	0	0	0	0	1	44	0	0	45	45		
Rhabdomyo sarcoma	0	1	0	2	0	0	3	0	1	0	1	0	17	0	4	17	21		
Other solid tumors	0	0	0	1	0	0	1	0	0	0	0	0	47	0	1	47	48		

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- & Acute myeloid leukemia,
- @ Acute lymphoblastic leukemia,
- + Chronic myeloid leukemia,
- % Myeloproliferative neoplasm,
- \$ Myelodysplastic syndrome,
- * Bone marrow,
- ^ Peripheral blood stem cells,
- # Cord blood