

# Current Uses and Outcomes of Hematopoietic Cell Transplantation (HCT) in the US: A 30,000 Foot View

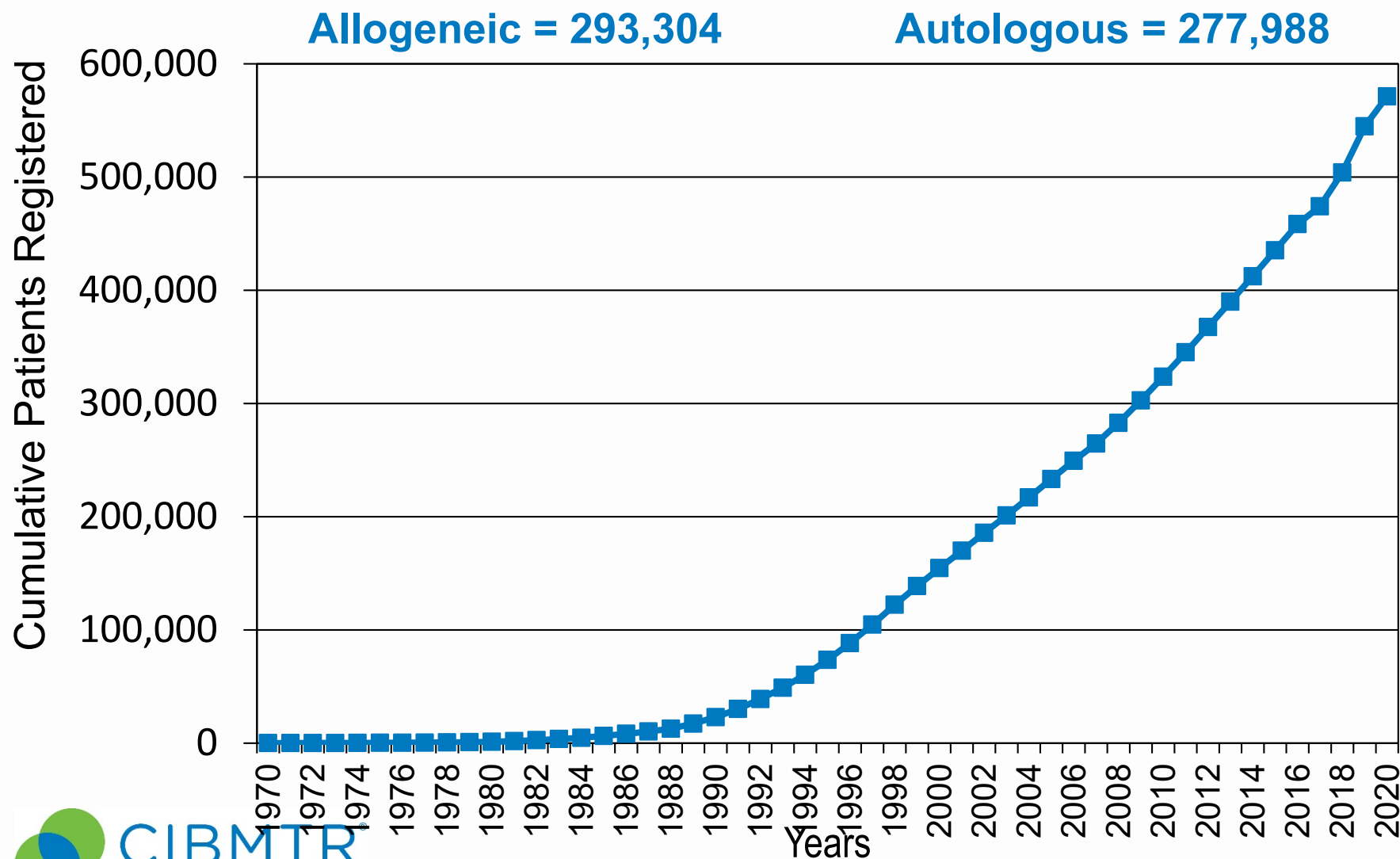
November 2021

## Disclosures

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- Research Support: Amgen, Astellas, Gamida Cell Ltd, Genentech, Magenta Therapeutics, Medac GmbH, Oncolmmune
- Consulting: Allovir, Medac GmbH

# CIBMTR: Research Affiliation of the Medical College of Wisconsin and the National Marrow Donor Program/Be The Match



- Funded by NIH and HRSA (and others)
- Multi-faceted research program with large outcomes registry
- Captures data on 100% of allogeneic and >90% of autologous HCTs in the US

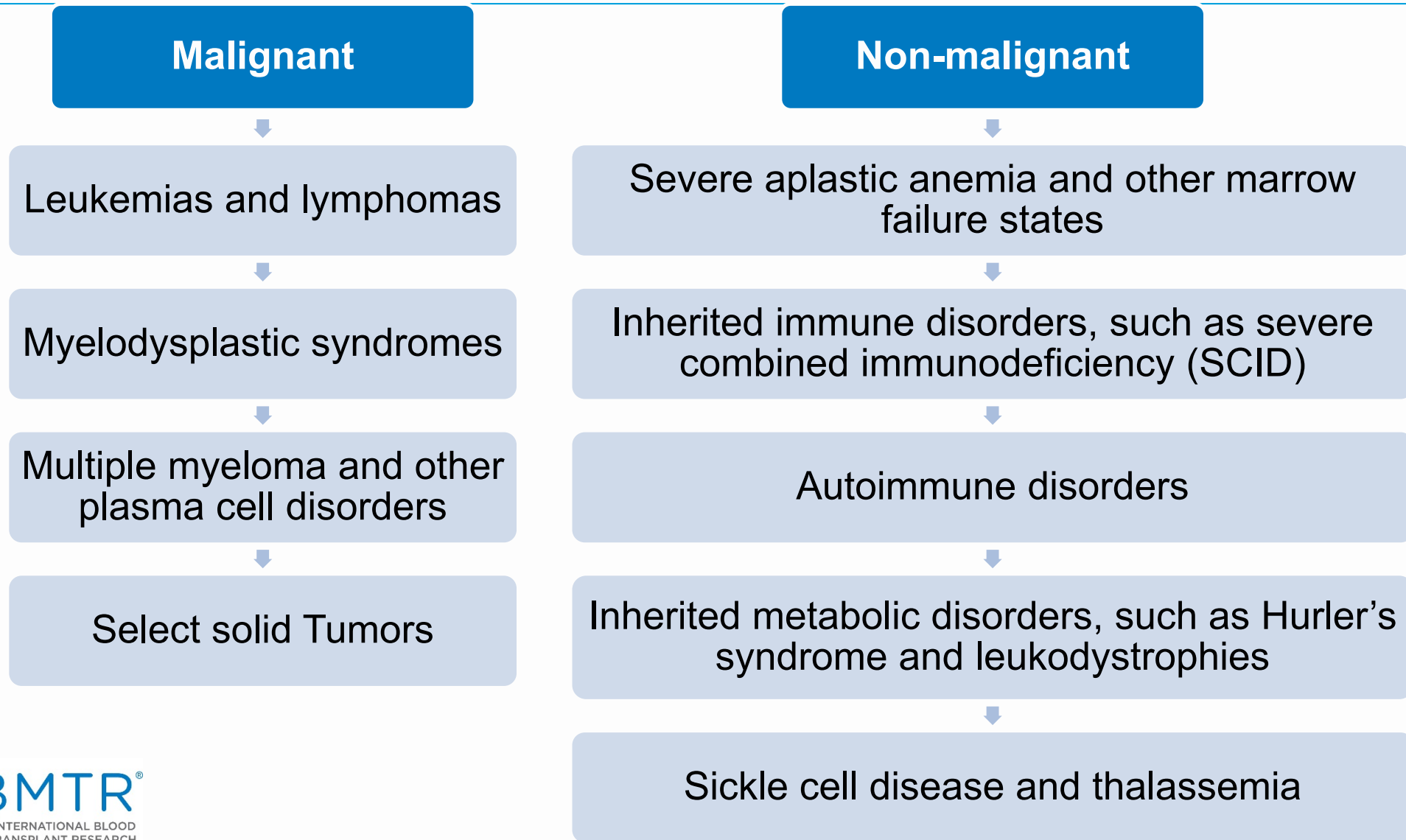
# What We Are Talking About:

## Hematopoietic Stem Cell Transplantation (HCT)

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- HCT is an intensive therapy used primarily for blood cancers as well as other uncommon bone marrow failure and immune deficiency disorders
- Cytotoxic/immune suppressive therapy followed by infusion of blood stem cells to:
  - Restore hematopoiesis destroyed by the primary disease and/or the pretransplant therapy given at high (myeloablative or marrow-killing) doses
  - Provide an immune-mediated graft-versus-malignancy effect

# Diseases Treatable by HCT



# What We Are NOT Talking About

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- There are many *other types* of stem cells
  - Embryonic stem cells
  - Other organ-specific stem cells, e.g. cardiac, retina, neuron – used for tissue regeneration
- There are *other uses* of hematopoietic stem cells
  - Immune modulation to facilitate kidney and other solid organ transplants
  - Gene therapy for congenital diseases
- These are diverse therapies, none of which are standard of care or done frequently.
  - Administered by diverse medical specialties
  - Different spectrum of therapeutic impacts and early/late adverse effects
  - VERY few data and almost no long-term data
- The type and extent of long-term disabilities that may ensue are still unknown but will certainly be different from those seen after HCT – and from each other.
  - The expertise to estimate these lies in the communities focused on the diseases for which the therapies are being developed

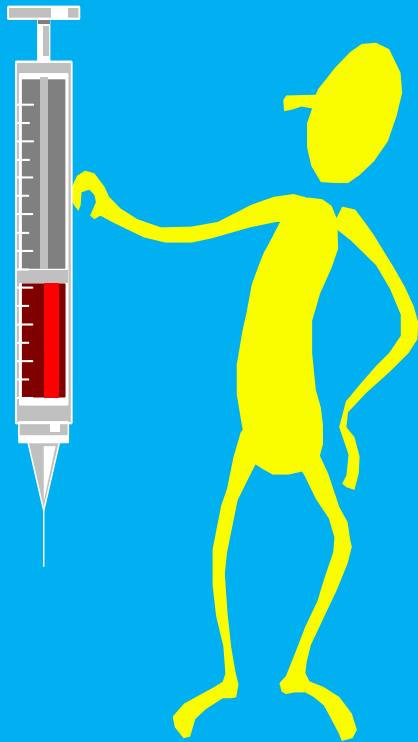
# Two Major Types of HCT

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- Autologous (from the patient)
  - Collected from the patient's bloodstream and stored for transplant
  - May be an option for patients with certain diseases where dose-intensification is the primary goal
- Allogeneic
  - Cells from a family member, unrelated donor or umbilical cord blood unit
  - Potential for potent immune-mediated anti-cancer effects
  - Requires (usually) close matching for HLA – cell surface proteins critical to immune responses
    - Multiple HLA loci (**HLA-A, B, C, DRB1**, DQ, DP) of varying importance

# Sources of Stem Cells

**Bone Marrow**



**Peripheral Blood**

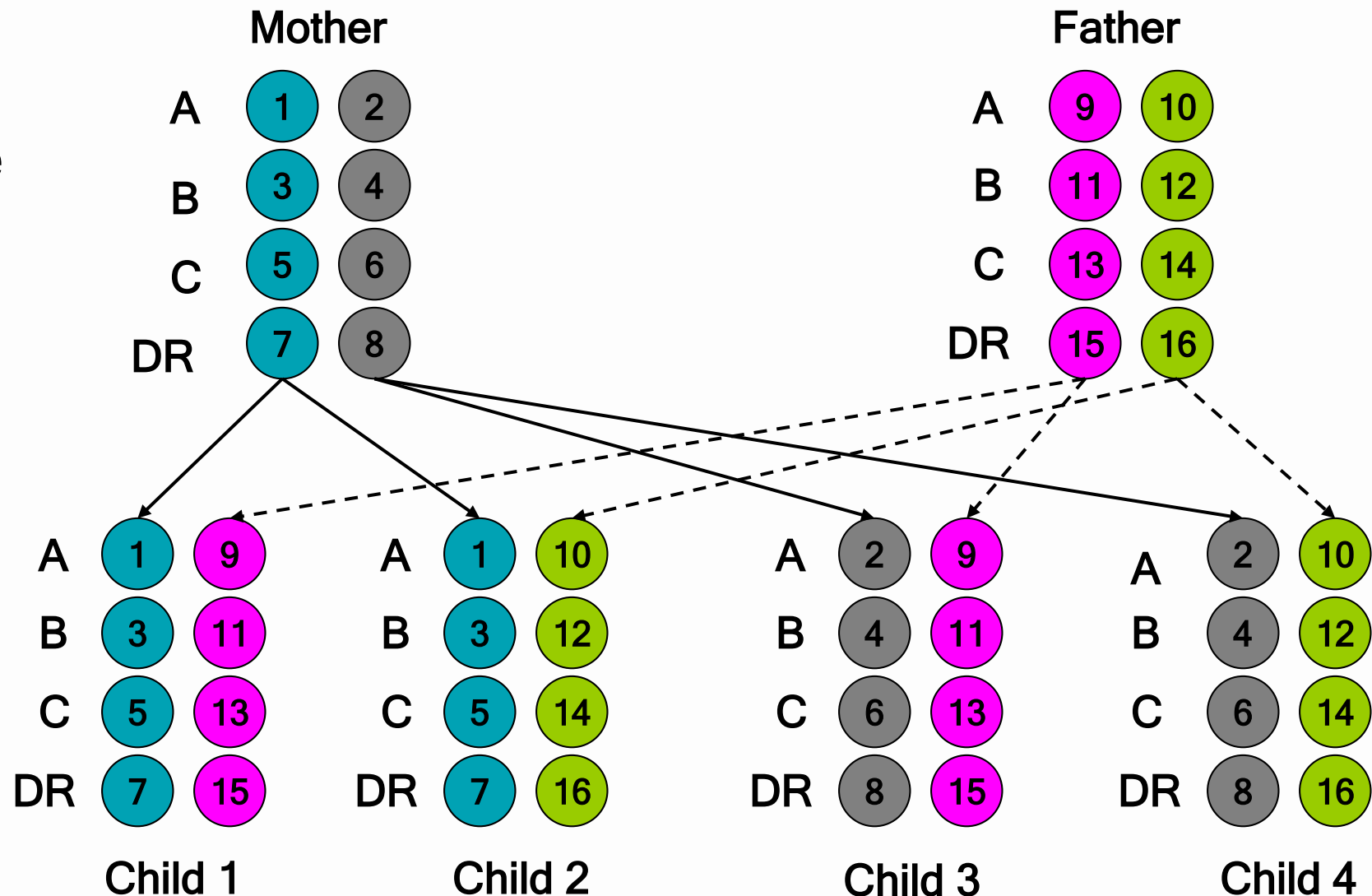


**Cord Blood**



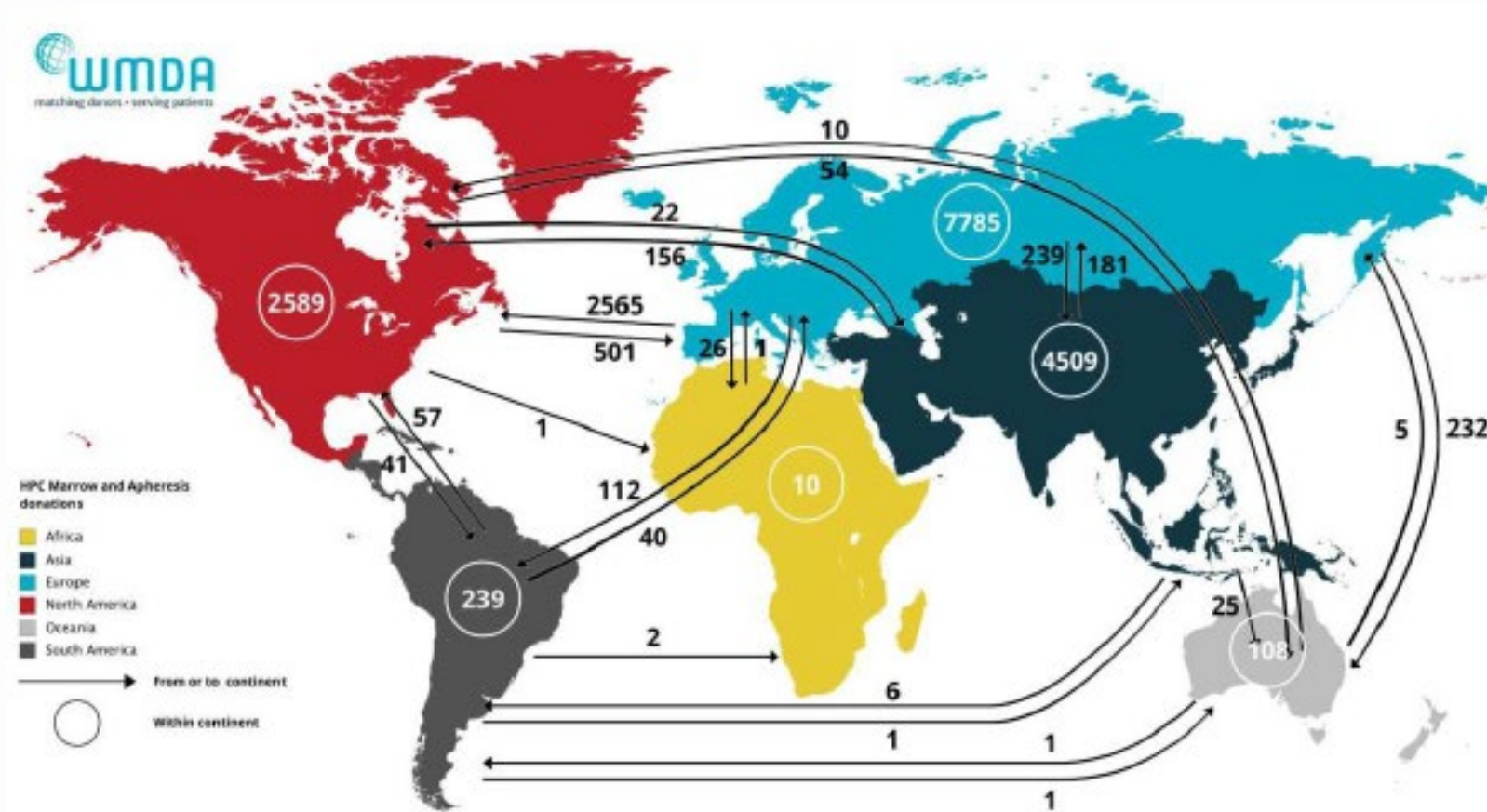
# HLA Inheritance: Half from your father, half from your mother

Only 30% of patients have an HLA-matched family member



# World Marrow Donor Association

wmda.info



38,127,657 unrelated donors

74 donor registries from 55 countries

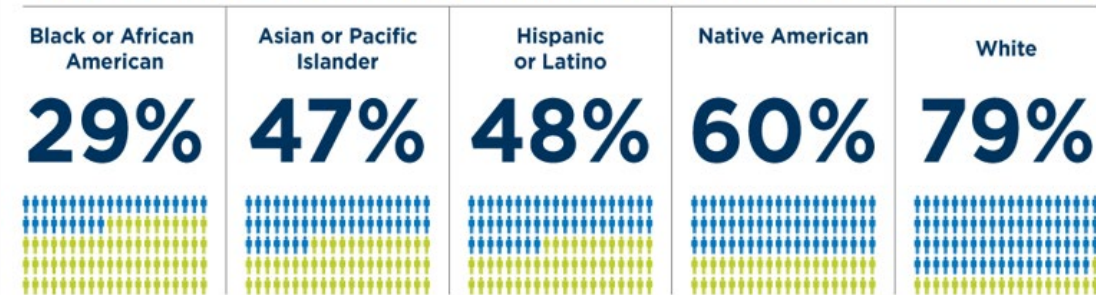
806,508 cord blood units

49 cord blood banks from 33 countries

# Donor Sources for Allogeneic HCT

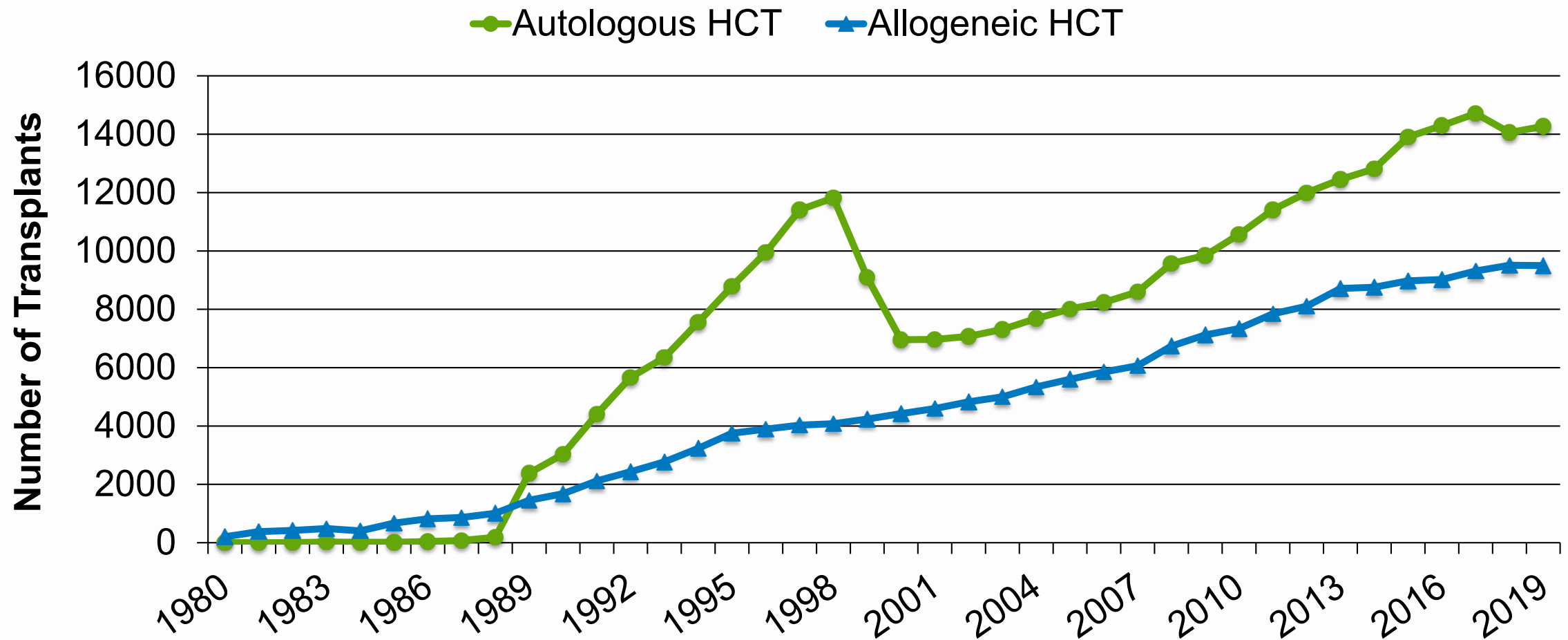
- Matched relative
  - 30% chance of full sibling match – GOLD Standard
- Matched unrelated donor
  - Chance related to ethnicity
- **Mismatched unrelated**
  - Donor who is < 8/8 HLA match with recipient
- **Mismatched (haploidentical) relative**
  - Related donor who shares on haplotype with the patient
- **Umbilical cord blood**
  - Stem cells collected from umbilical cord + placenta after baby is born; immaturity of immune system allows for higher level of HLA mismatch

## ODDS OF FINDING A MATCH BASED ON ETHNIC BACKGROUND

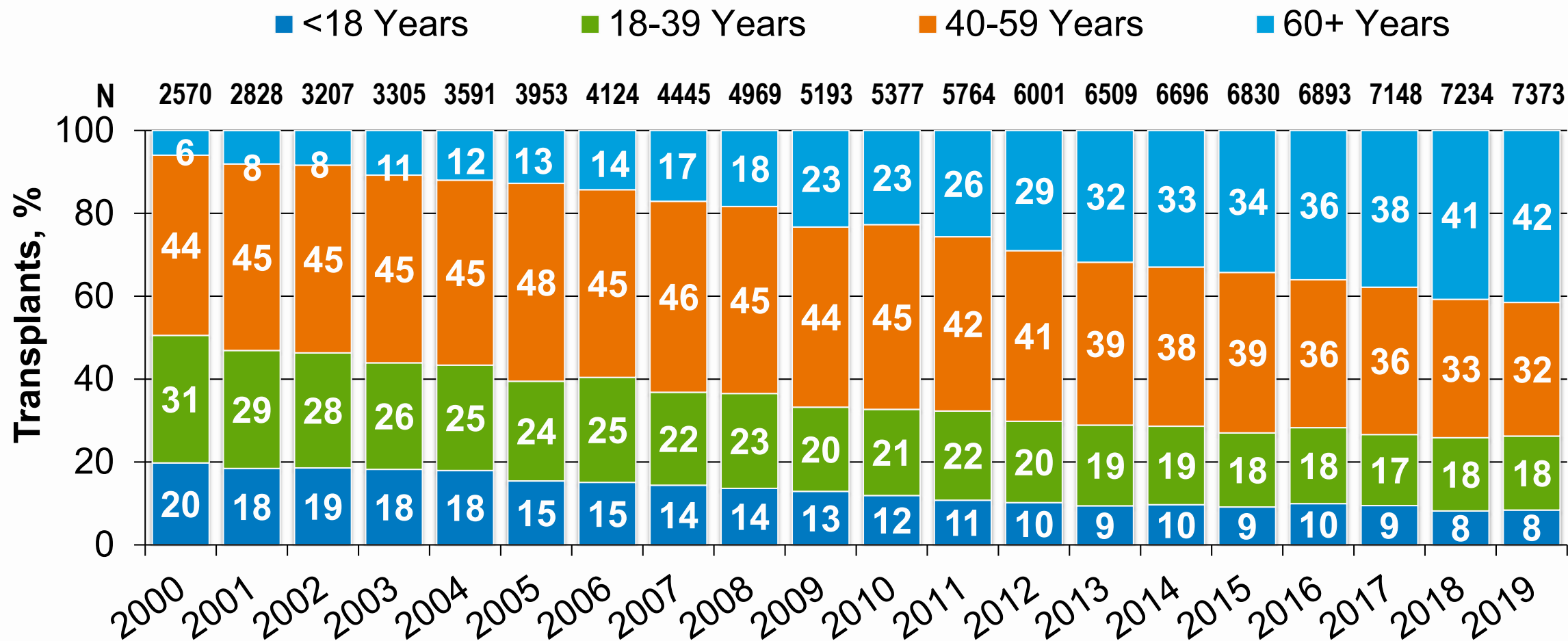


# Annual Number of HCT Recipients in the US by Transplant Type

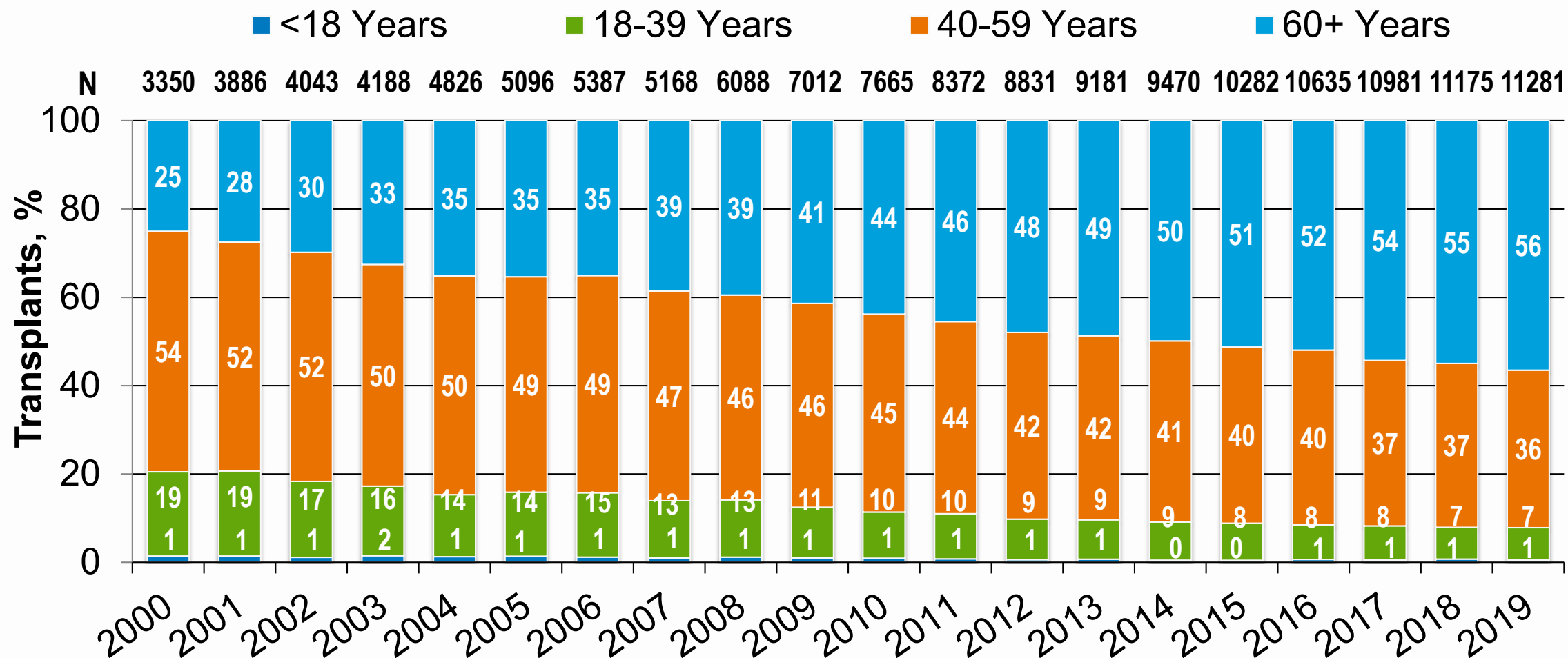
<https://www.cibmtr.org/ReferenceCenter/SlidesReports/SummarySlides>



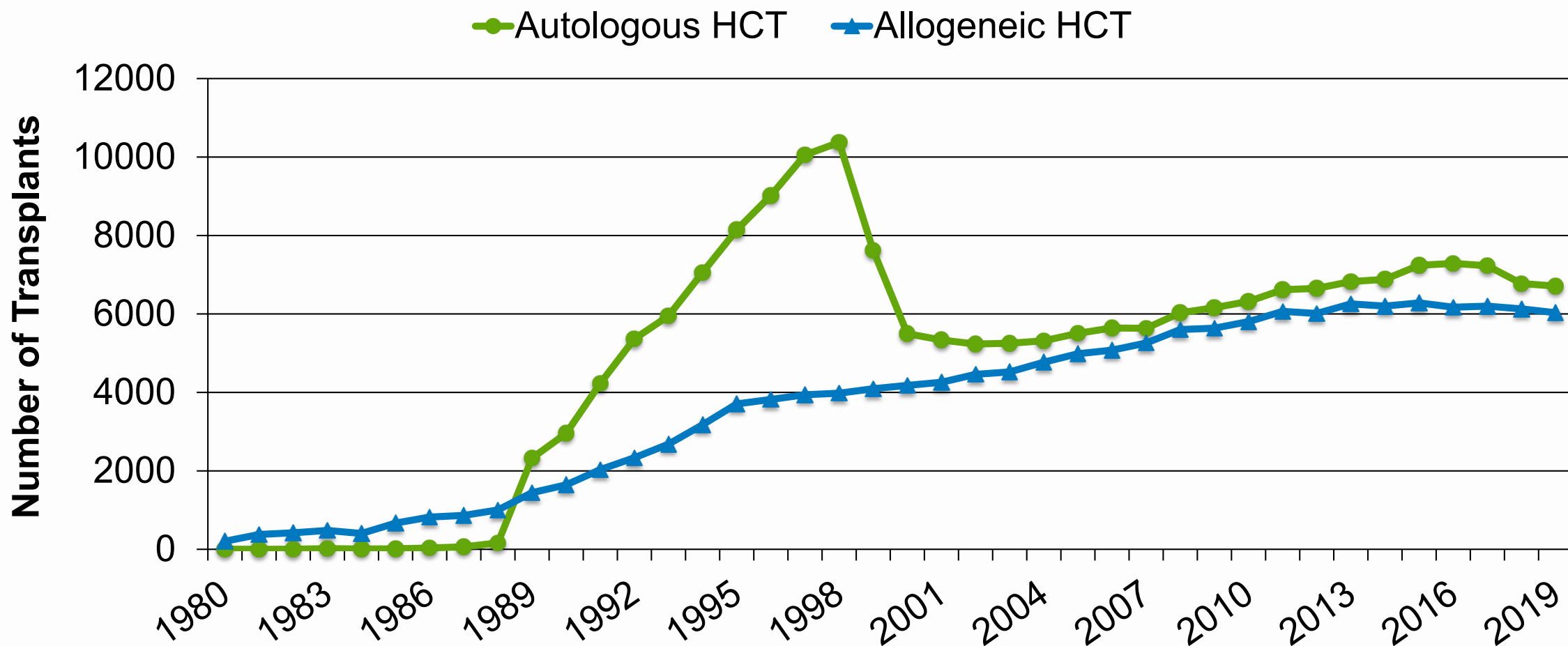
# Trends in Allogeneic HCT in the US by Recipient Age



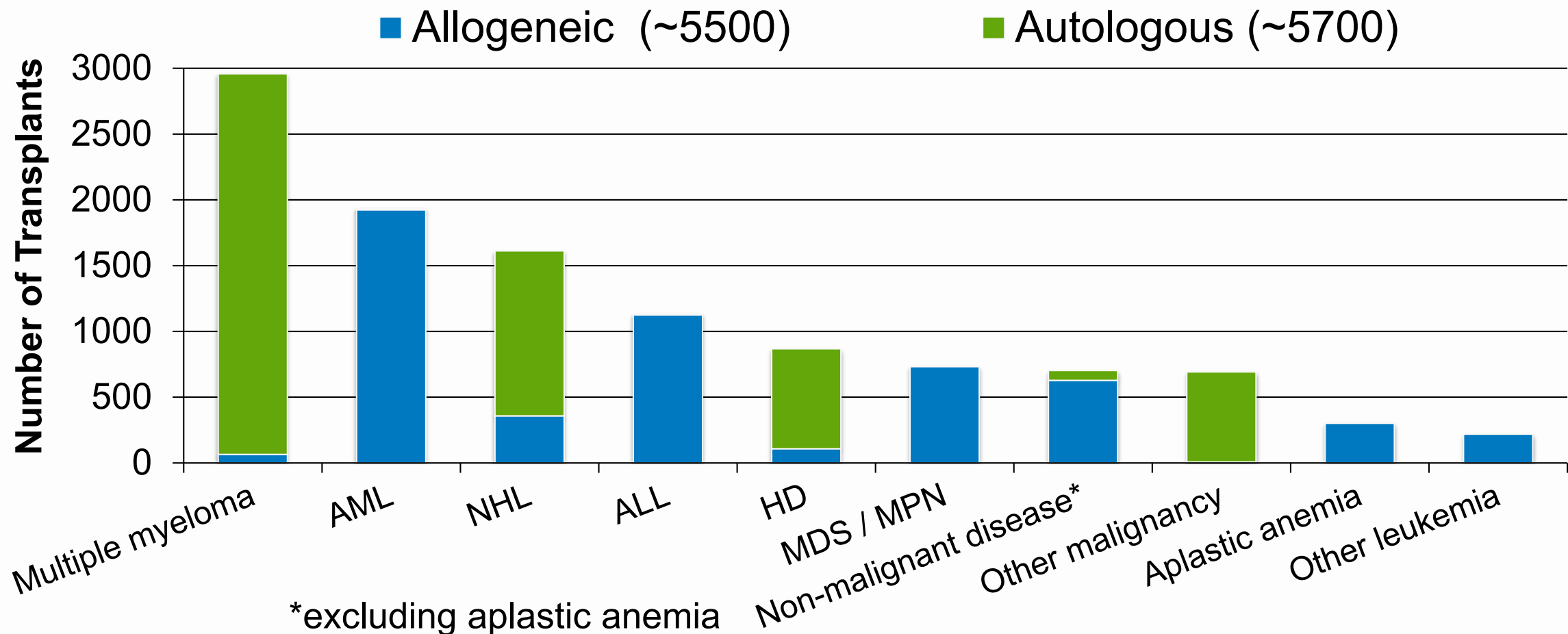
# Trends in Autologous HCT in the US by Recipient Age



# Estimated Annual Number of HCT Recipients in the US by Transplant Type, Age <60 Years

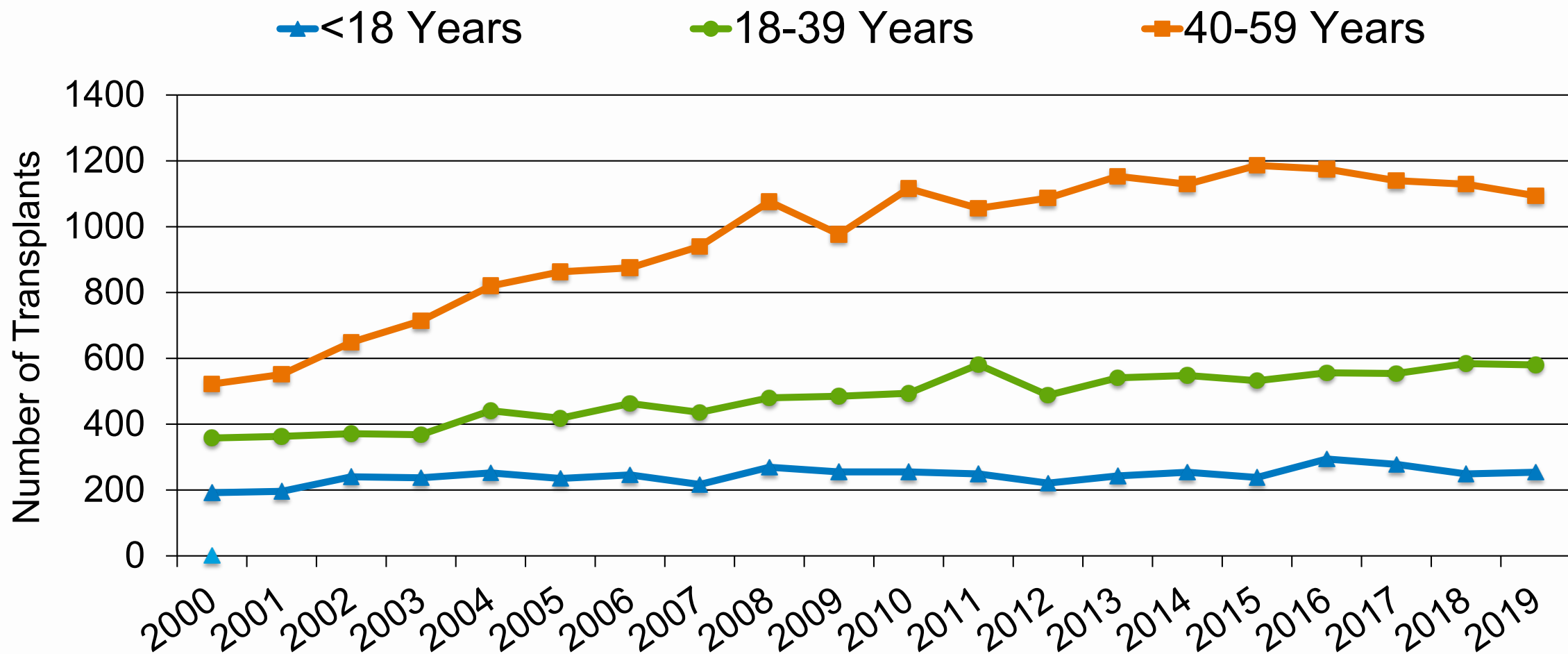


# Indications for Hematopoietic Cell Transplant in the US, 2019, Age <60 Years

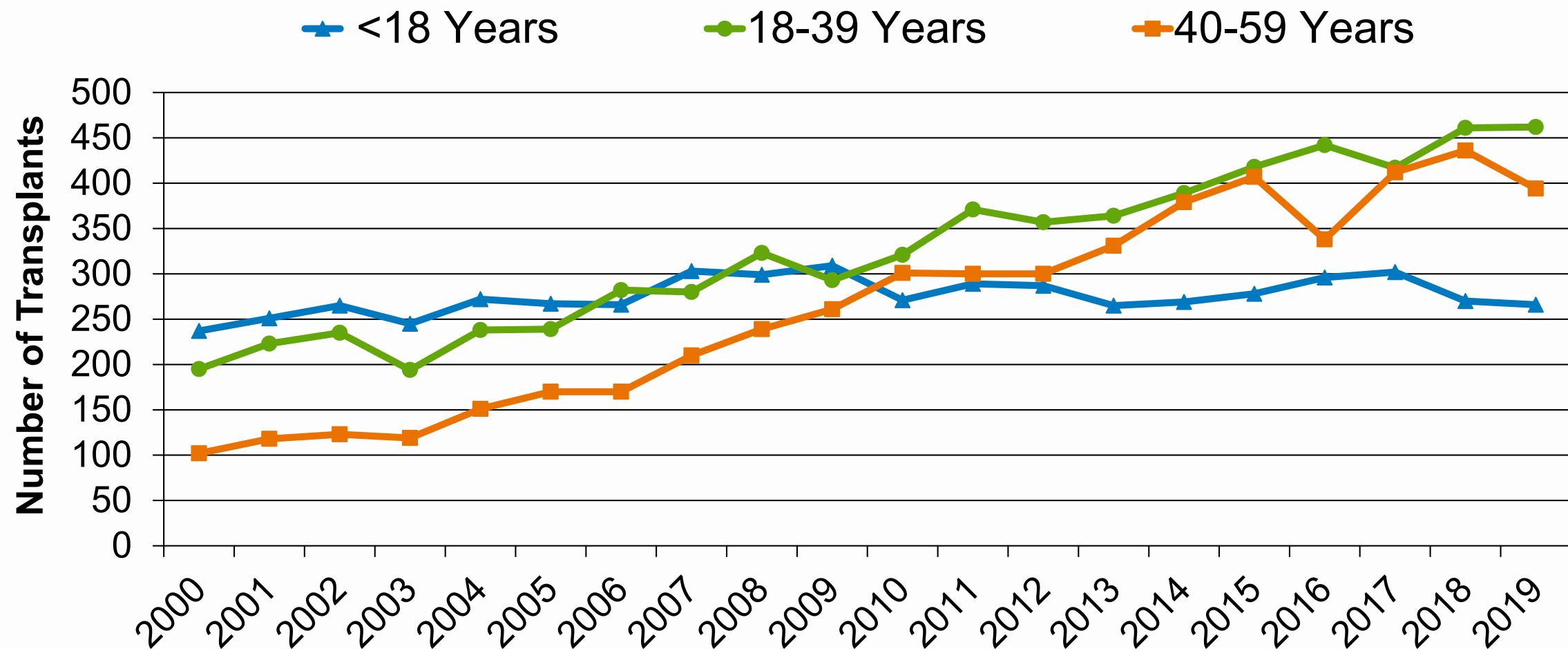


AML= acute myeloid leukemia; NHL=non-Hodgkin lymphoma; ALL= acute lymphoblastic leukemia; HD=Hodgkin disease; MDS= myelodysplastic syndrome; MPN=myeloproliferative disease

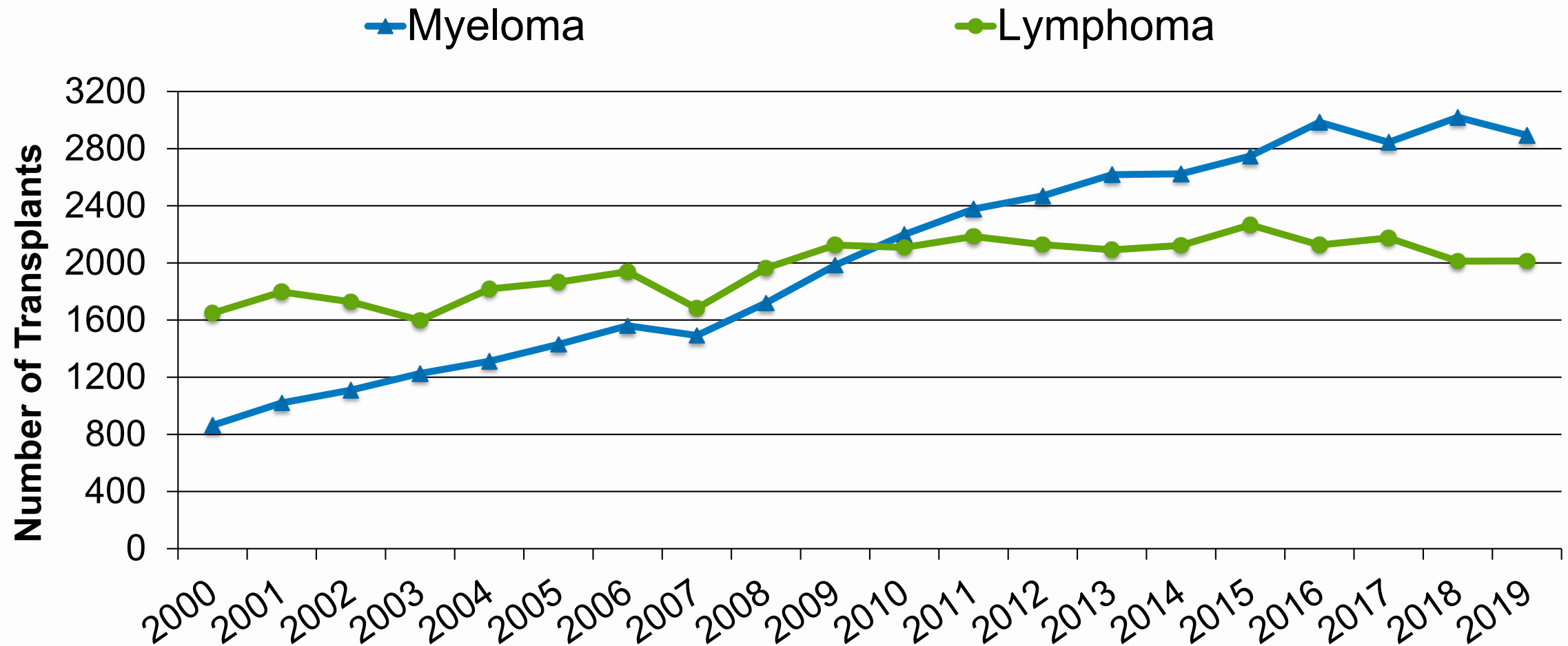
# Trends in Allogeneic HCT for Acute Myelogenous Leukemia (AML) in the US, by Recipient Age



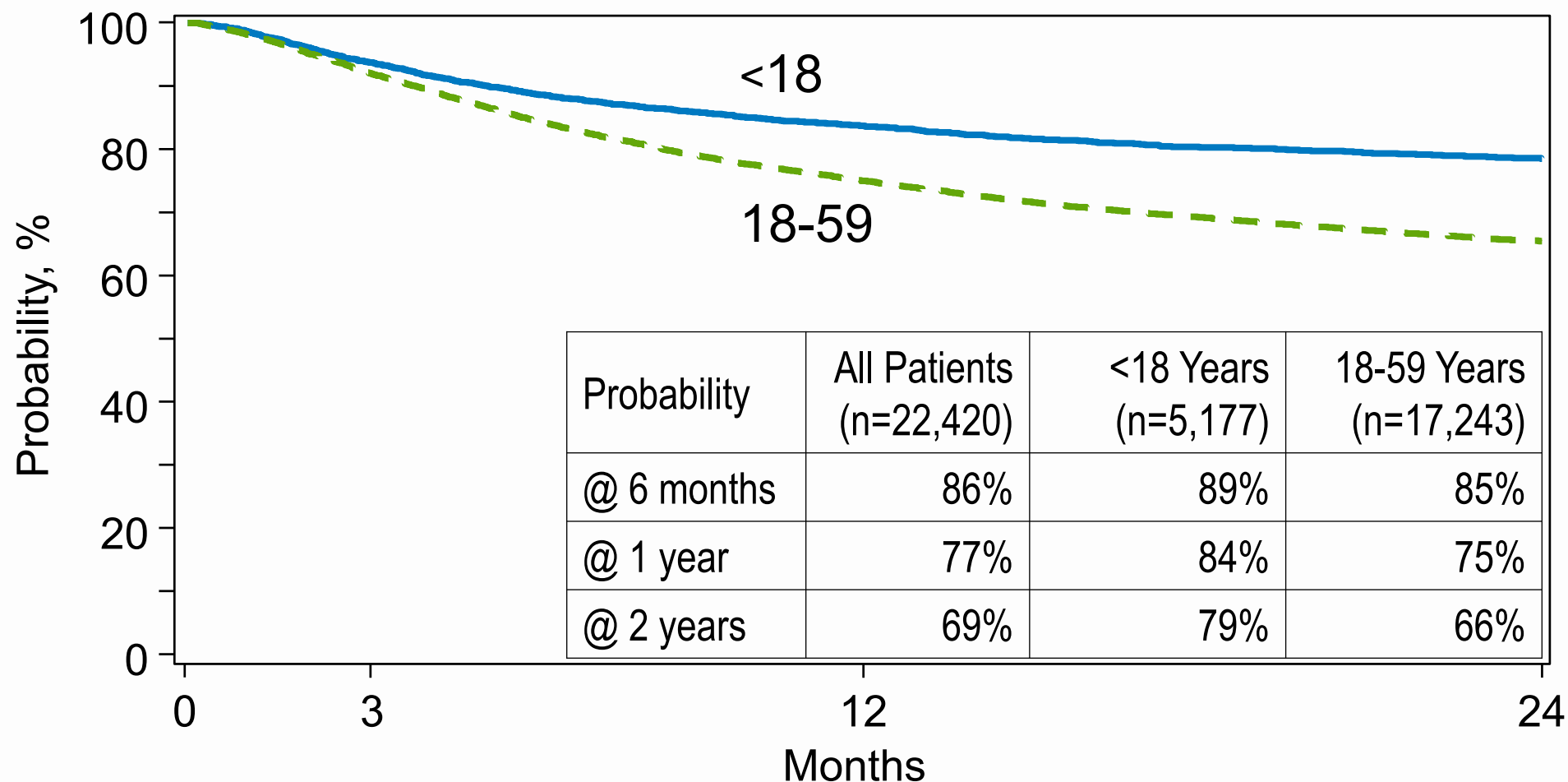
# Trends in Allogeneic HCT for Acute Lymphoblastic Leukemia (ALL) in the US, by Recipient Age



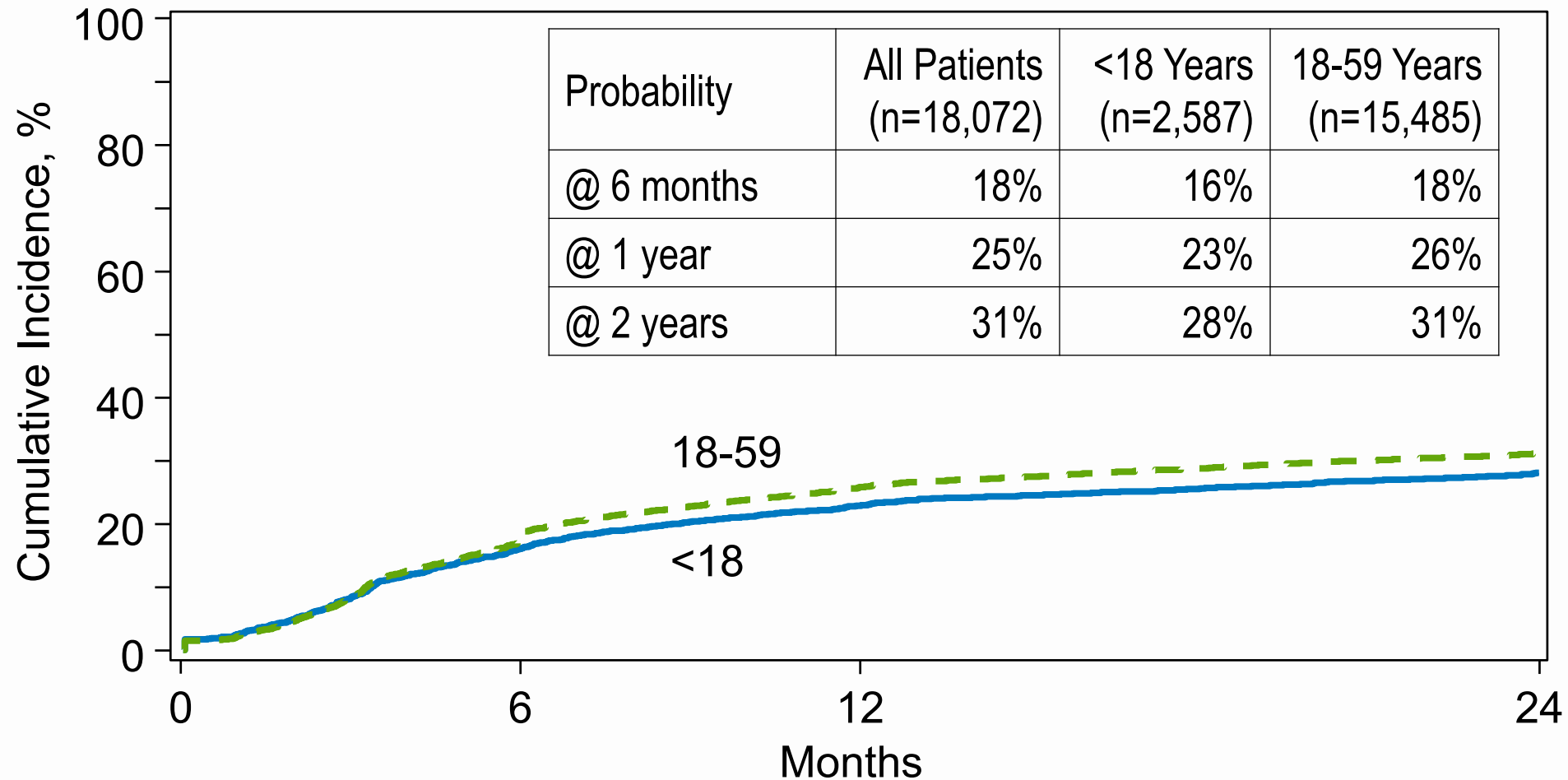
# Trends in Autologous HCT for Multiple Myeloma and Lymphoma in the US, Adults <60 Years



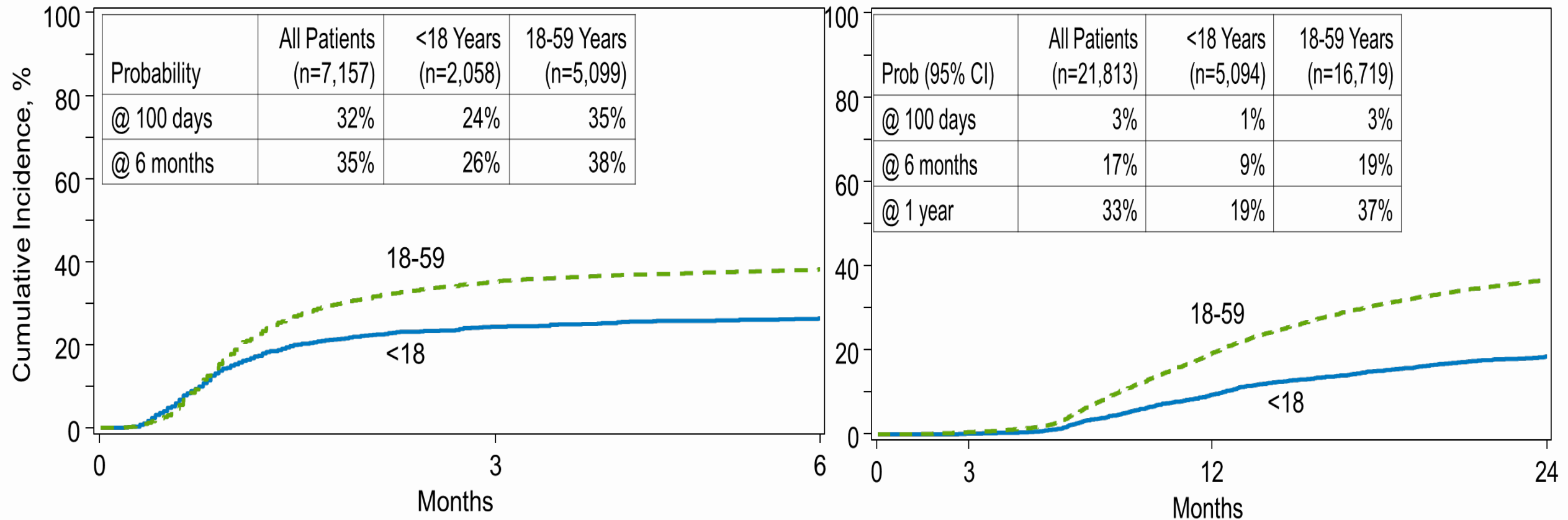
# Overall Survival After Allogeneic HCT for US Patients, Age <60 Years, 2015-2019



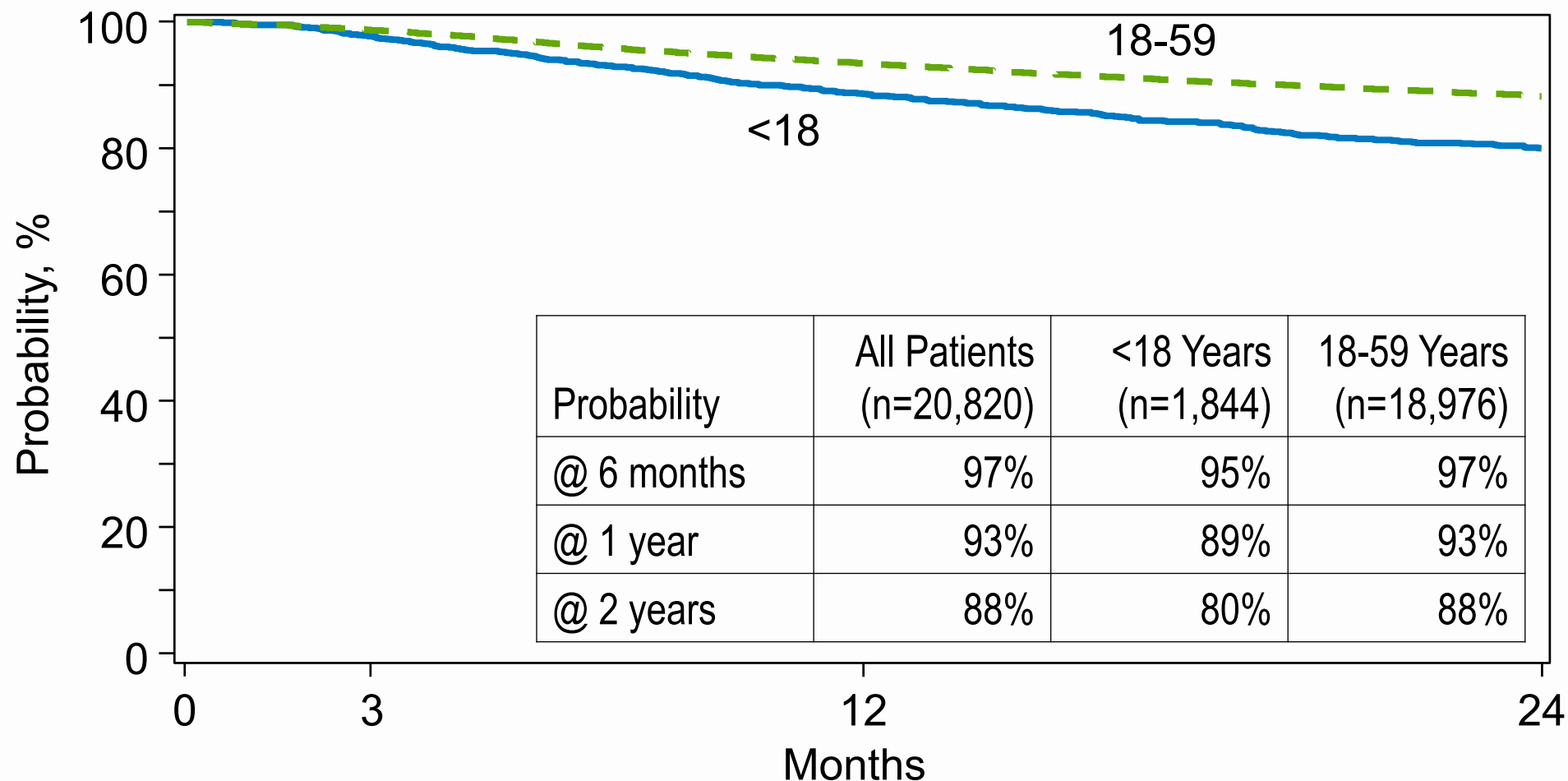
# Relapse / Progression After Allogeneic HCT for Hematologic Malignancies in US Patients, Age <60 Years, 2015-2019



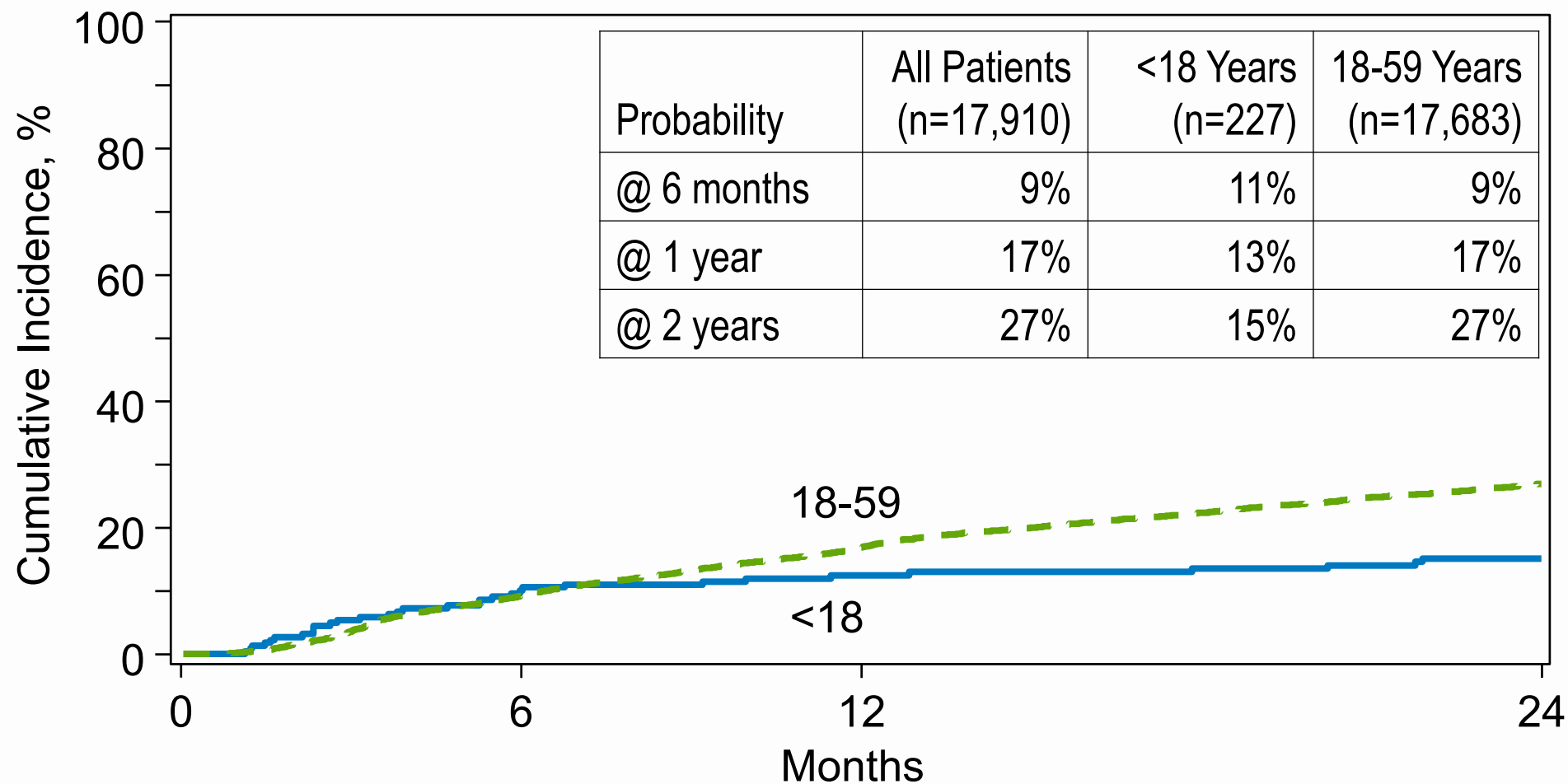
# Grade II-IV acute GVHD and Moderate-Severe Chronic GVHD after Allogeneic HCT for US Patients, Age <60 Years, 2015-2019



# Overall Survival After Autologous HCT for US Patients, Age <60 Years, 2015-2019



# Relapse / Progression after Autologous HCT for Hematologic Malignancies in US Patients, Age <60 Years, 2015-2019

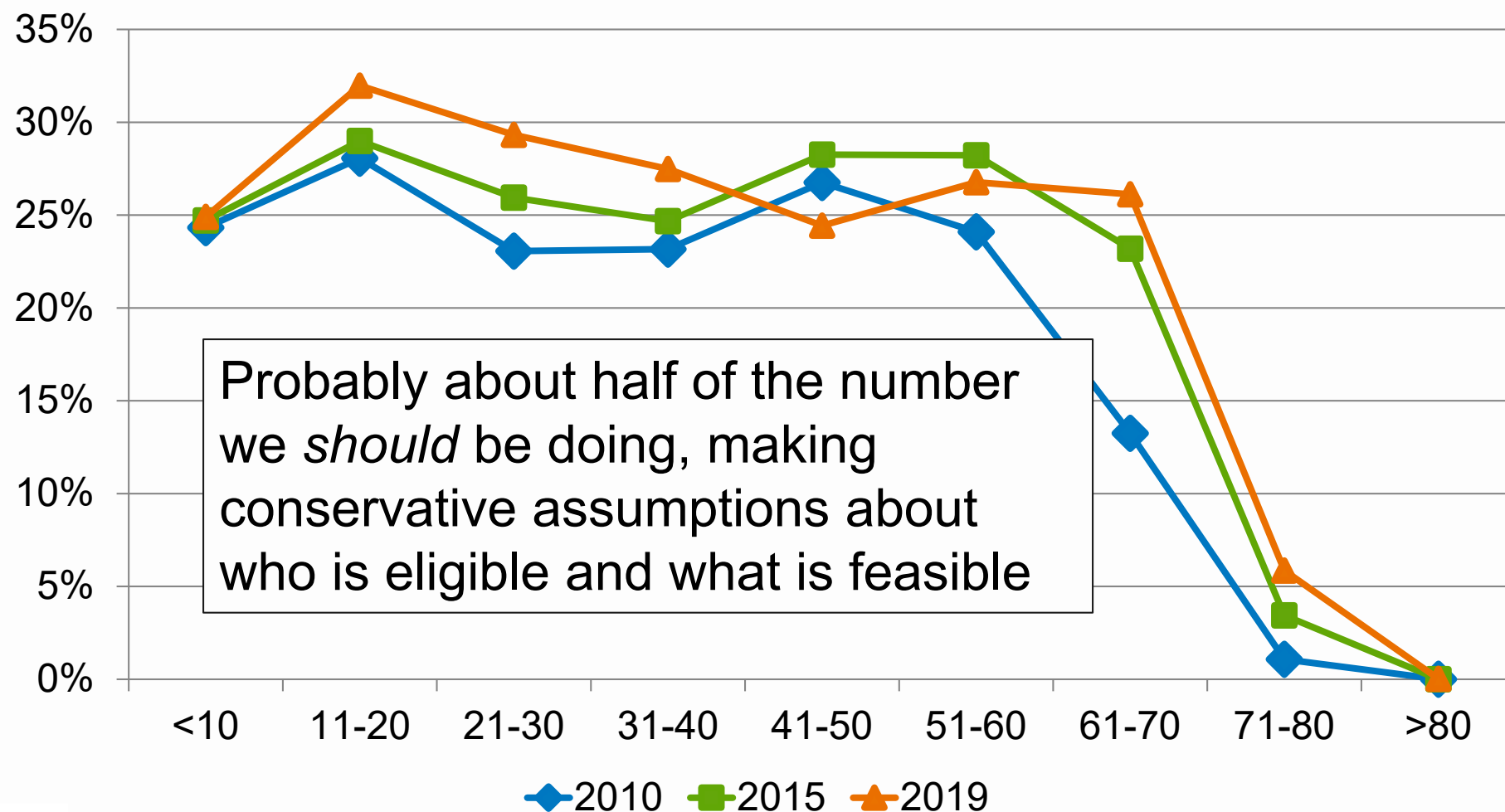


# The Numbers

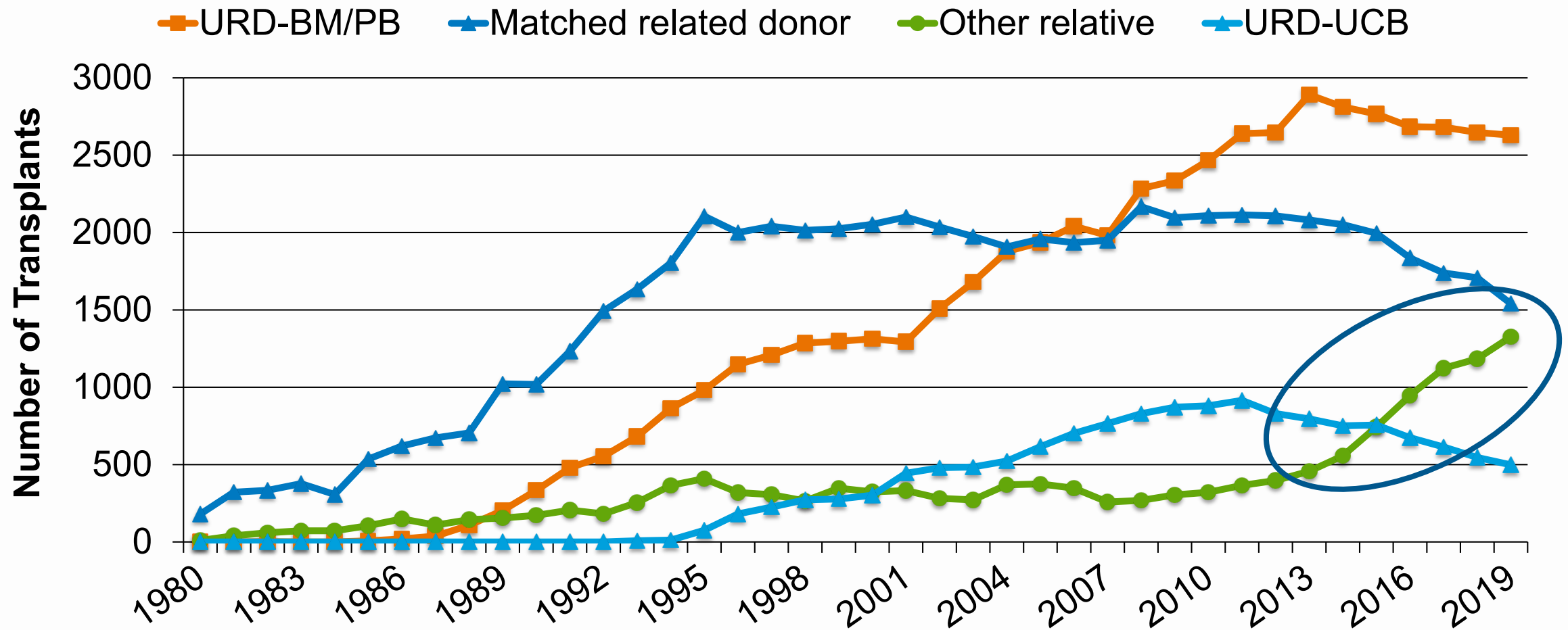
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- 11-12,000 HCTs yearly in patients younger than 60 years
  - ~20% of allo recipients and ~10% of auto recipients will die in the first year after transplant and another 10% in the second year
  - ~20% will relapse in the first year and another 5-10% in the second year (and will likely be disabled because of the need for further therapy)
  - About 30% of allotransplant recipients will develop significant chronic GVHD (with some having significant and prolonged morbidity)
  - The trajectory of survivors (with and without chronic GVHD) will be discussed by Dr. Lee
  - How much might this change in the next five years?

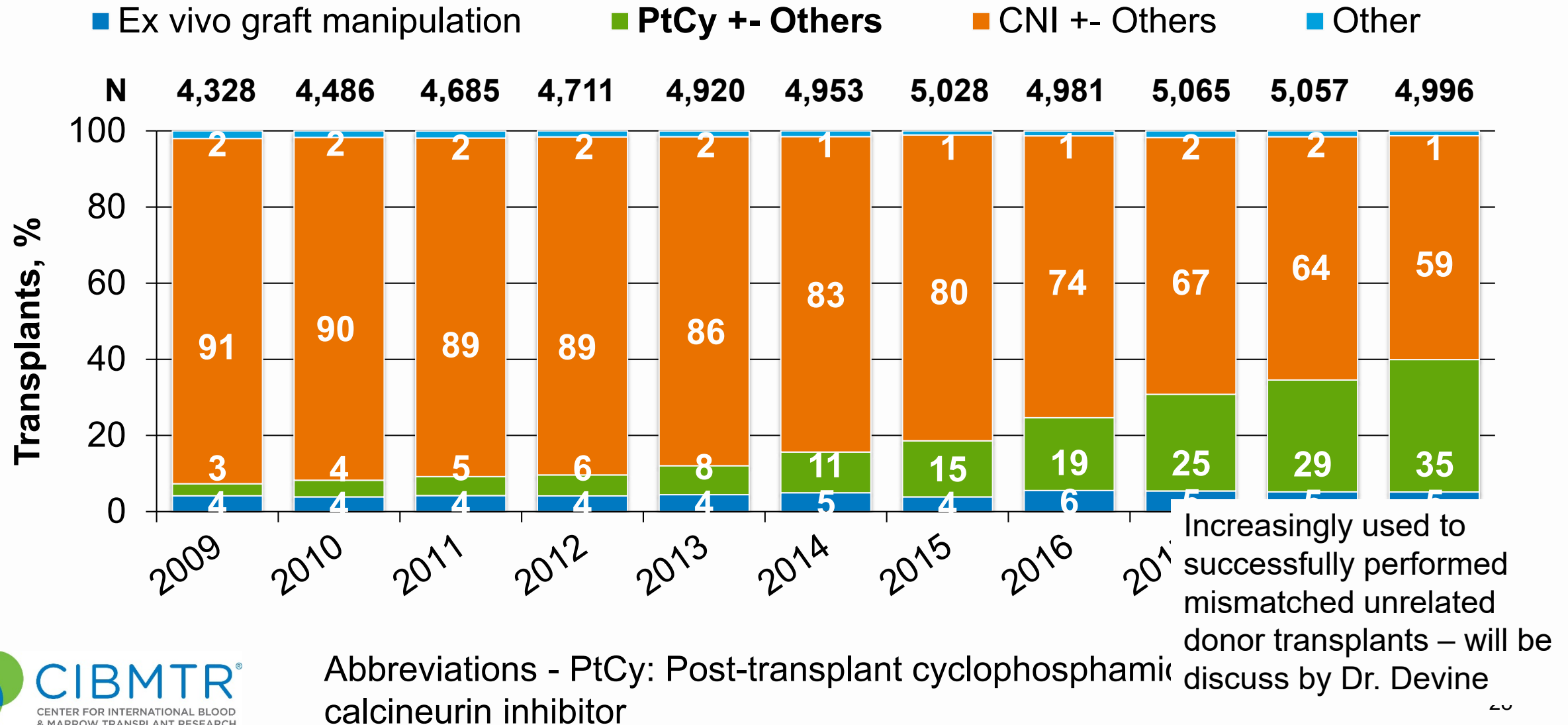
# HCT is Currently Under-Used: Proportion of AML Patients Transplanted by Age and Time Period



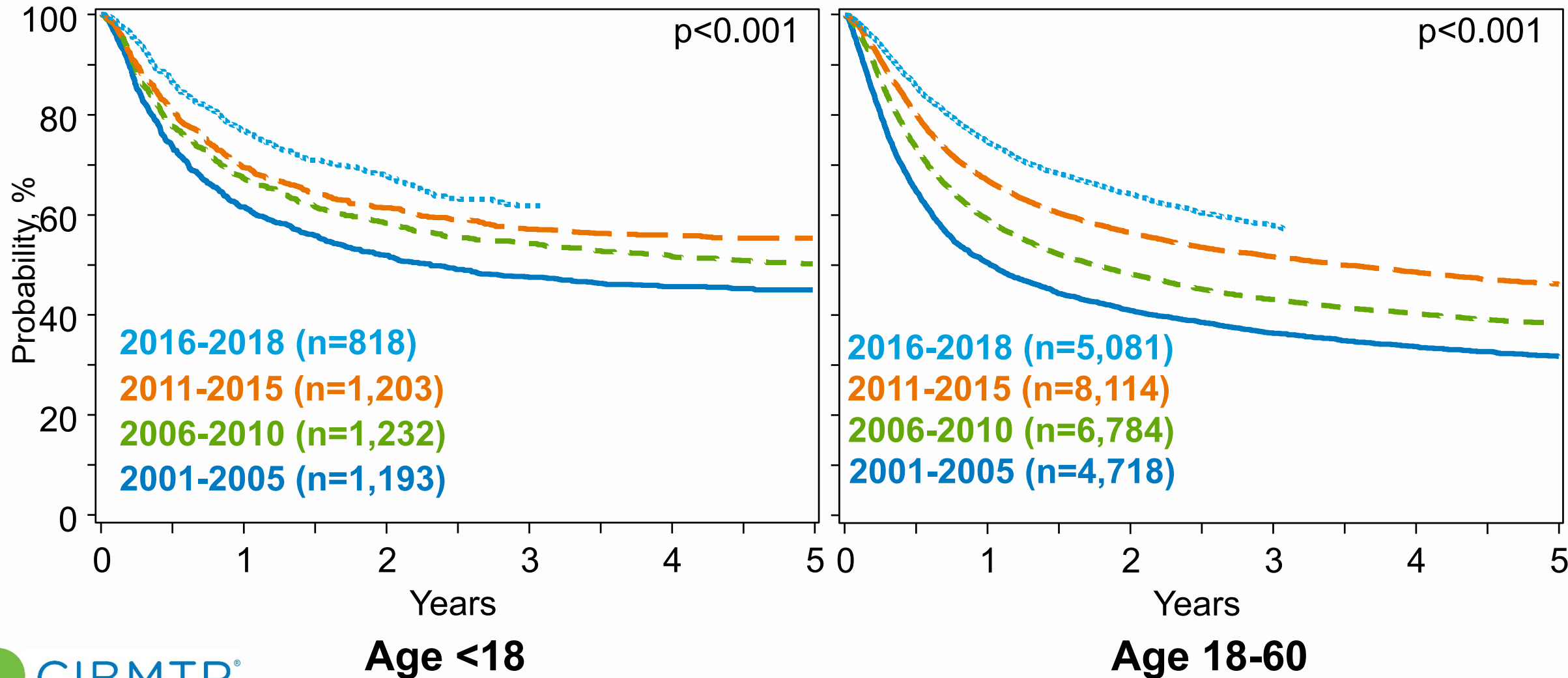
# Estimated Allogeneic HCT Recipients in the US by Donor Type, Age <60 Years



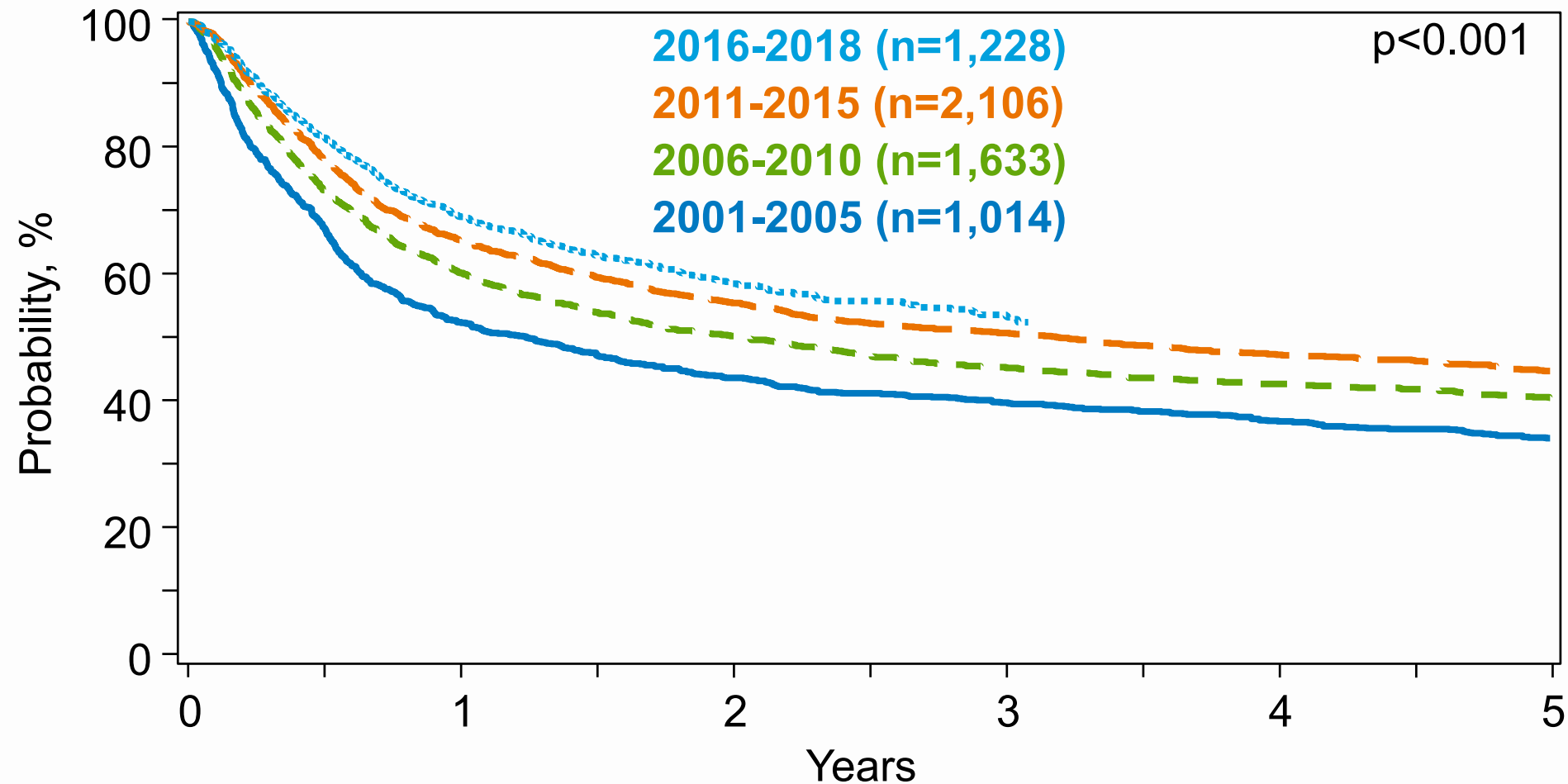
# HCT Recipients in the US by GVHD Prophylaxis, Age <60 Years: A Changing Standard of Care



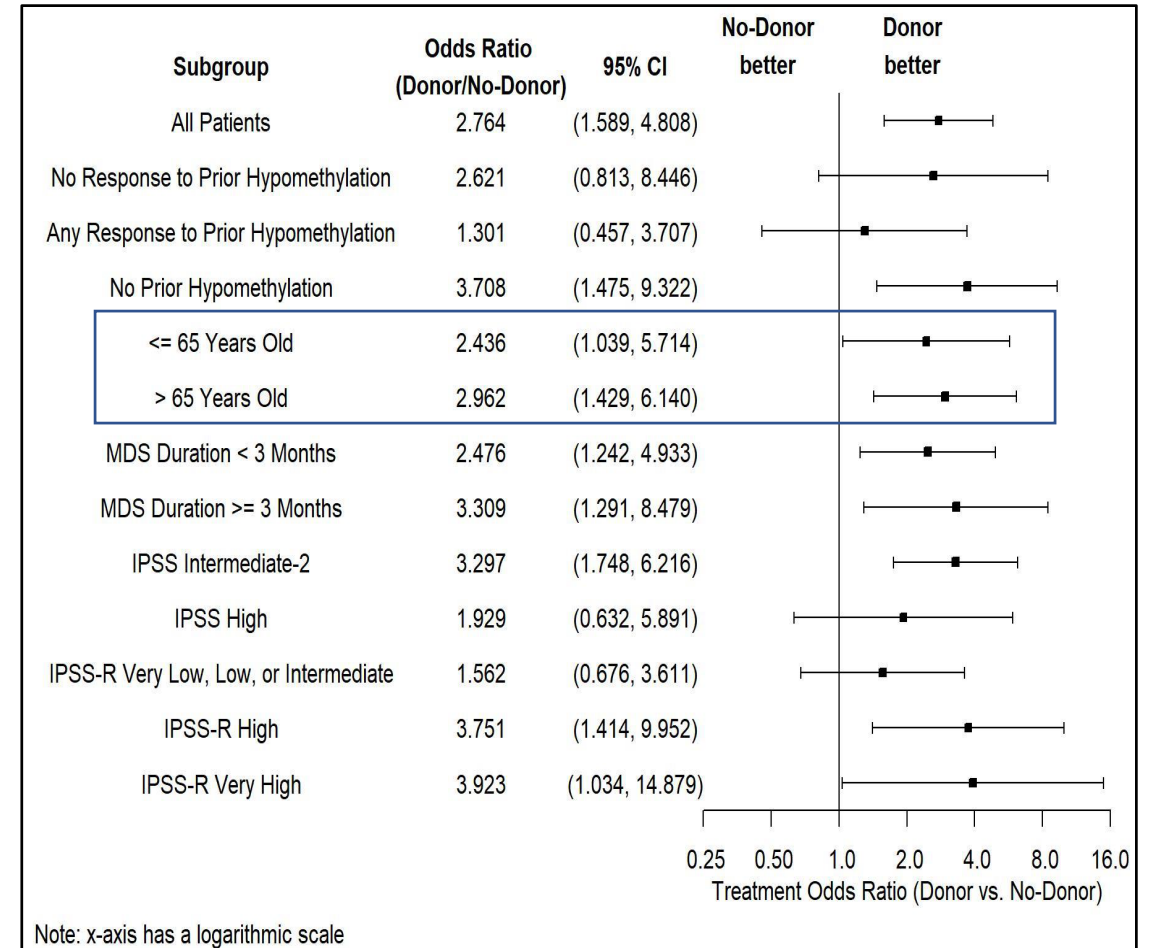
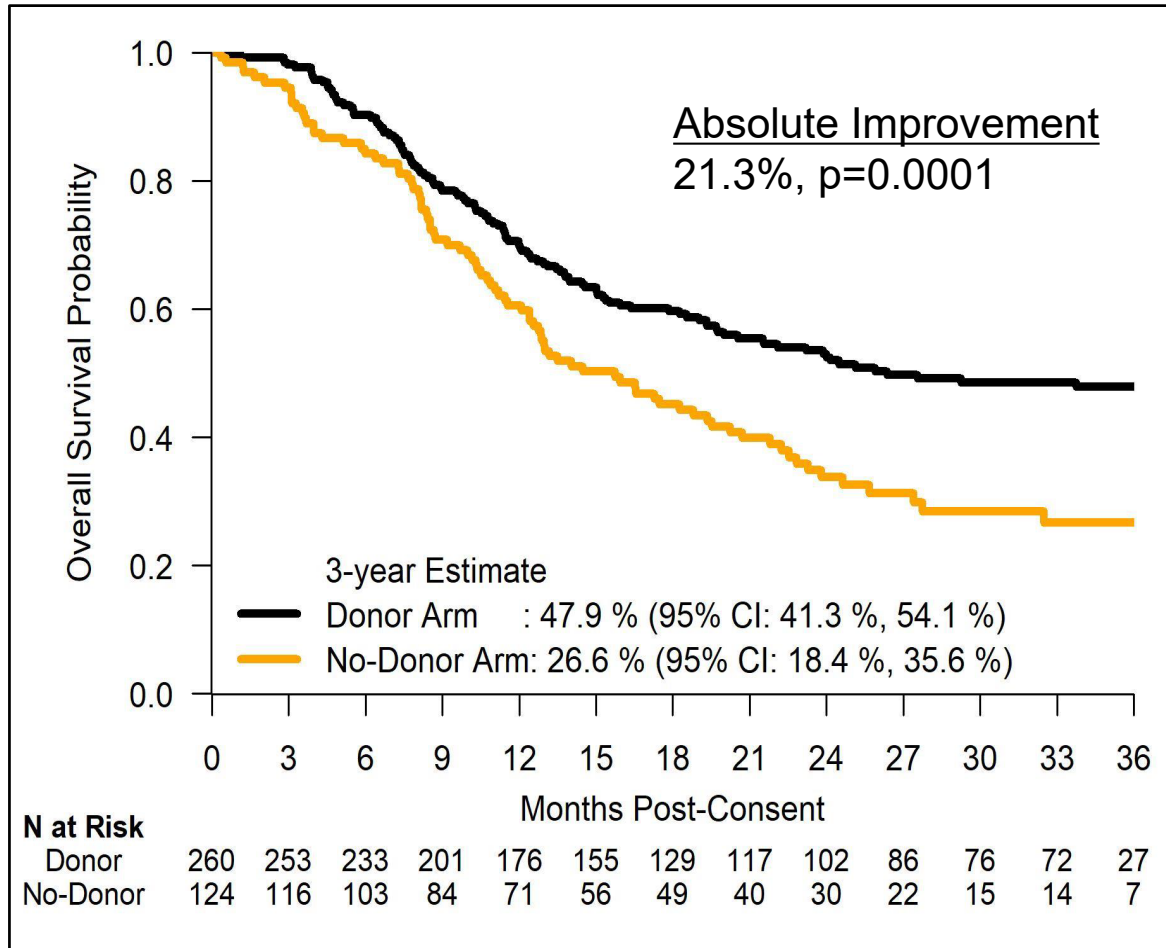
# Trends in Survival after Allogeneic HCT for Acute Myelogenous Leukemia, Age <60 Years, in the US, 2001-2018



# Trends in Survival after Allogeneic HCT for Myelodysplastic Syndrome, Age 18-59 Years, in the US, 2001-2018

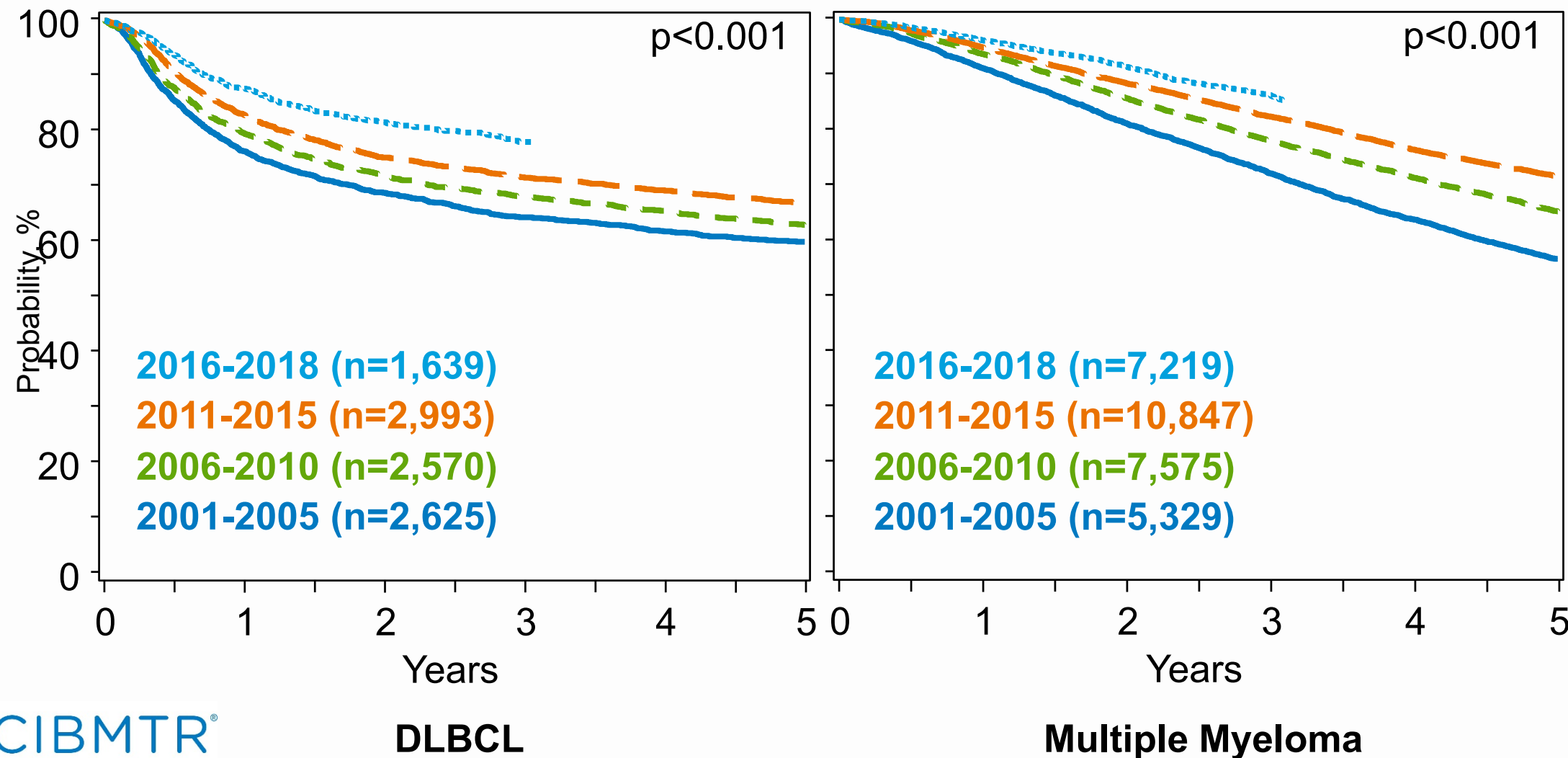


# BMT CTN 1102: HCT vs non-HCT Therapy: Significant Survival Advantage with HCT



Nakamura, Saber, et al. J Clin Oncol 2021

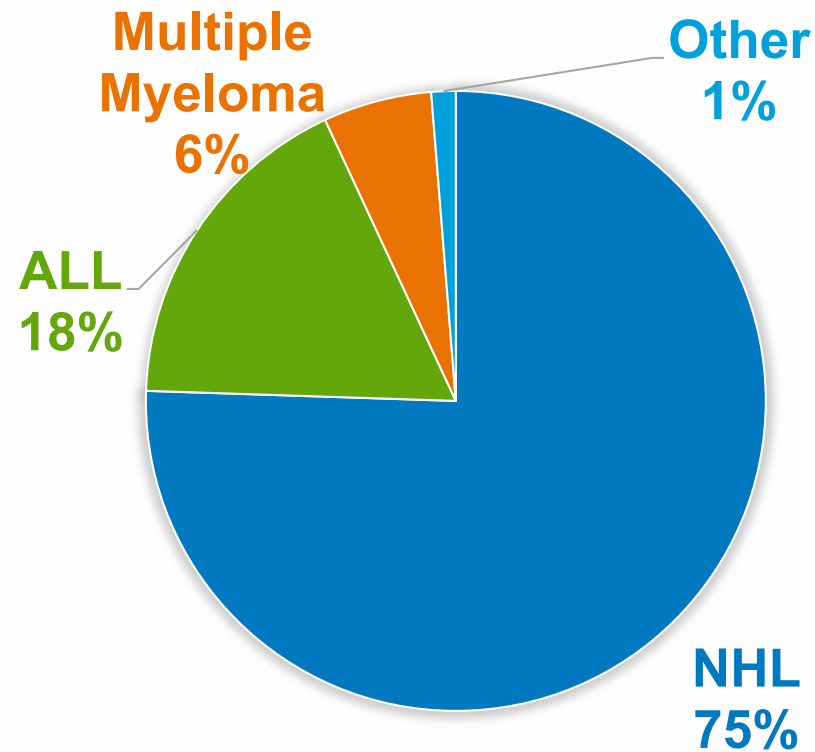
# Trends in Survival after Autologous HCT for Diffuse Large B-Cell Lymphoma (DLBCL) and Multiple Myeloma, Age <60 Years, in the US, 2001-2018



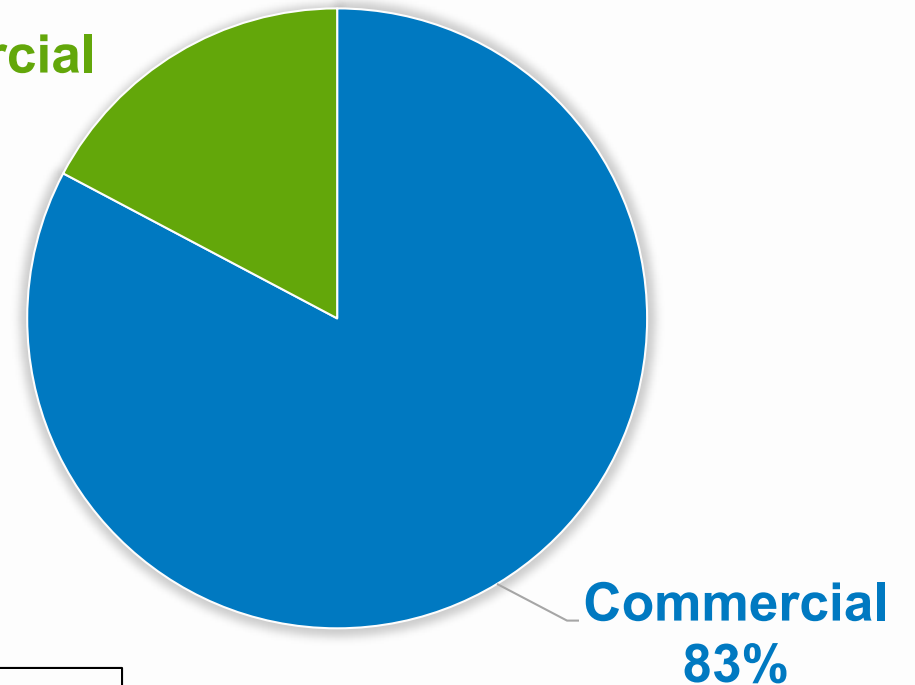
# Chimeric Antigen Receptor (CAR) T Cell Indications: 2016-2021 (N=5,364)



CELLULAR IMMUNOTHERAPY DATA RESOURCE

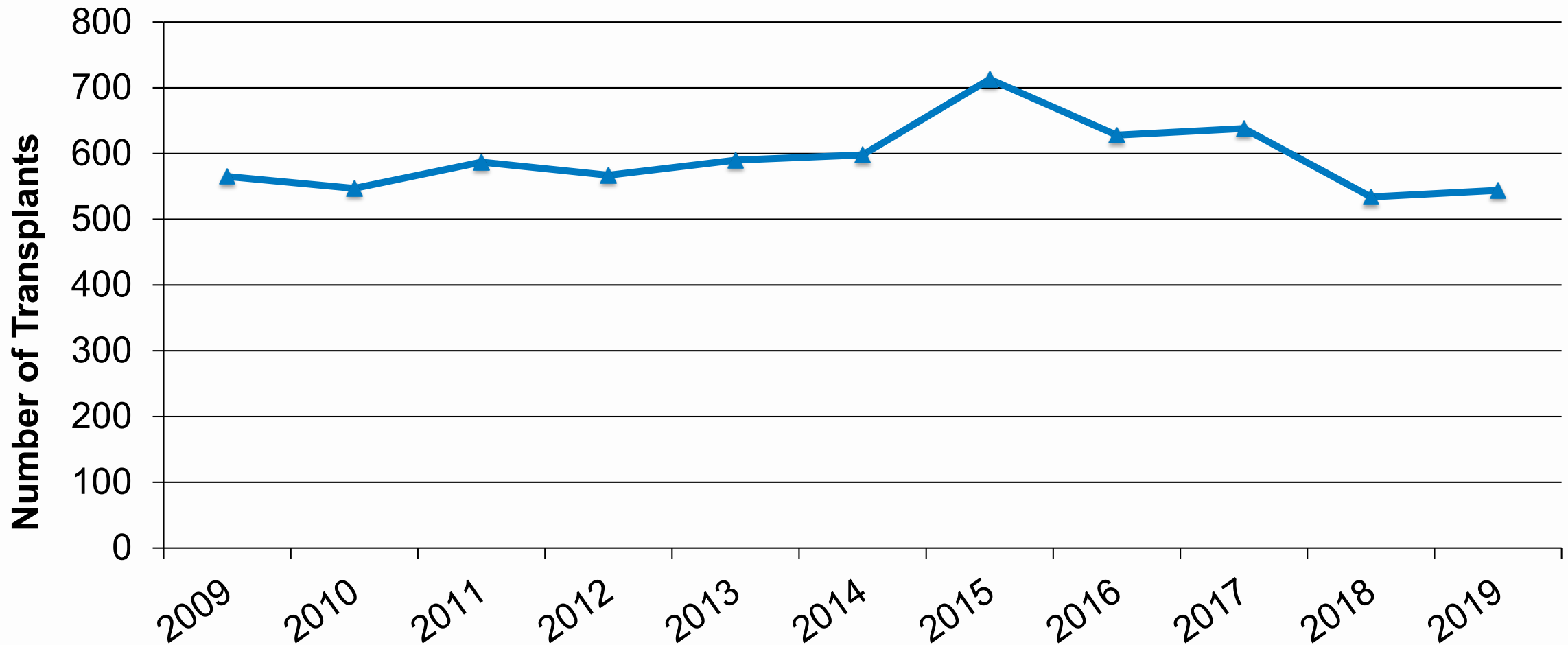


Noncommercial  
17%



Centers: 184 (US 95%)  
Median age: 60 y (<1-91)y  
Prior HCT: 33%

# Trends in Use of Autologous HCT for Diffuse Large B-Cell Lymphoma (DLBCL) in the US, Age <60 Years



# Summary

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- HCT is an effective therapy for patients with a wide range of hematologic disorders, primarily blood cancers
- Survival rates are increasing but mortality (and morbidity) from the procedure and recurrence of the underlying disease are still substantial
- Recent developments may increase use in some diseases and decrease use in others and affect the prevalence of some post-HCT complications