Iowa Oncology Society 2024 Best of ASCO

Trends in Hematopoietic Cell Transplantation in Acute Myeloid Leukemia from 2004-2020

Aditya Ravindra MD
Hematology & Medical Oncology Fellow

Mentor: Prajwal Dhakal MD

IOWA HEALTH CARE
Holden Comprehensive Cancer Center

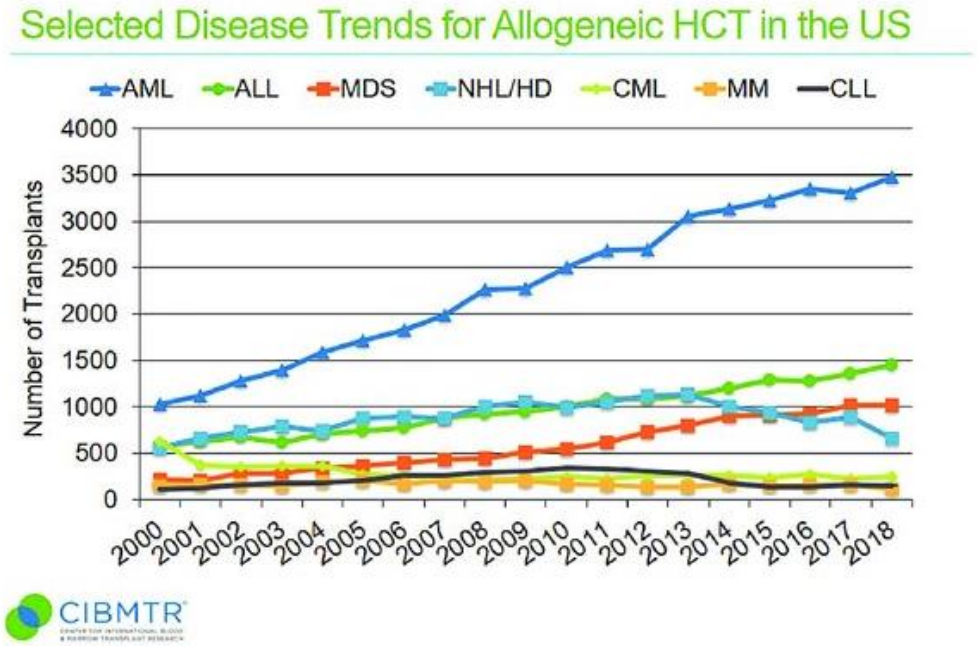
Financial Disclosures

This work was supported by clinical research funds from the Holden Comprehensive Cancer Center

Background

Hematopoietic Cell Transplantation in AML

- AML is the most common indication for allogenic HCT
- Allogenic HCT is the only curative therapy for patients with primary refractory AML
- HCT continues to become safer and more accessible

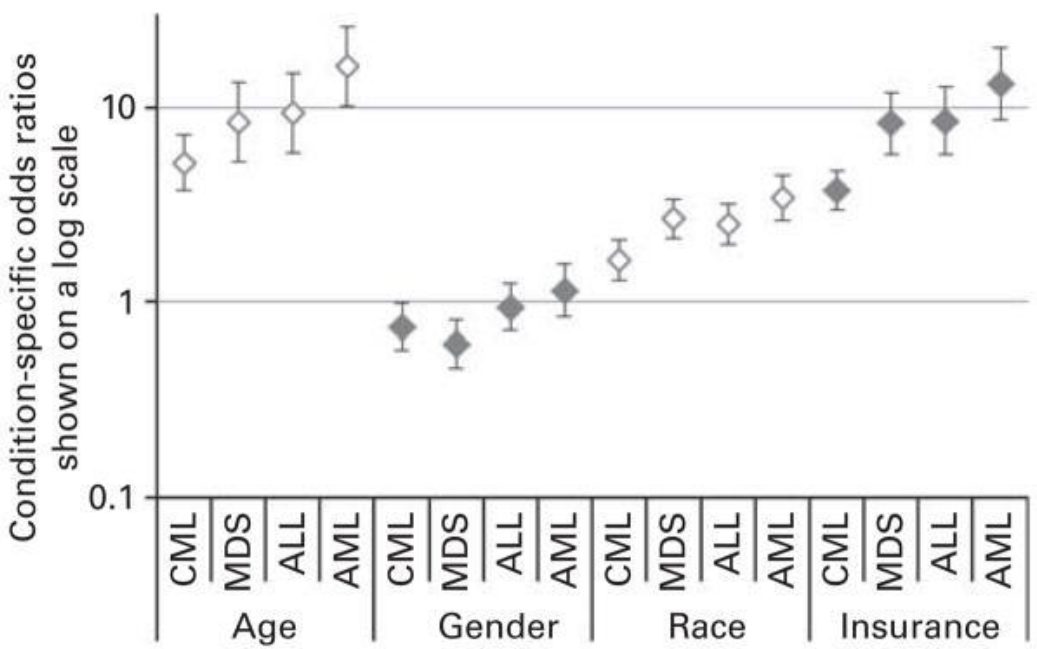


Granot, *et al*. History of hematopoietic cell transplantation: Challenges and progress.

IOWA

Barriers to HCT

- Despite its benefits in AML, HCT still remains underutilized
  - Biological factors of exclusion
    age, co-morbidities, AML subtype, race
  - Non-biological factors of exclusion
    educational status, income, insurance, distance to treatment facility

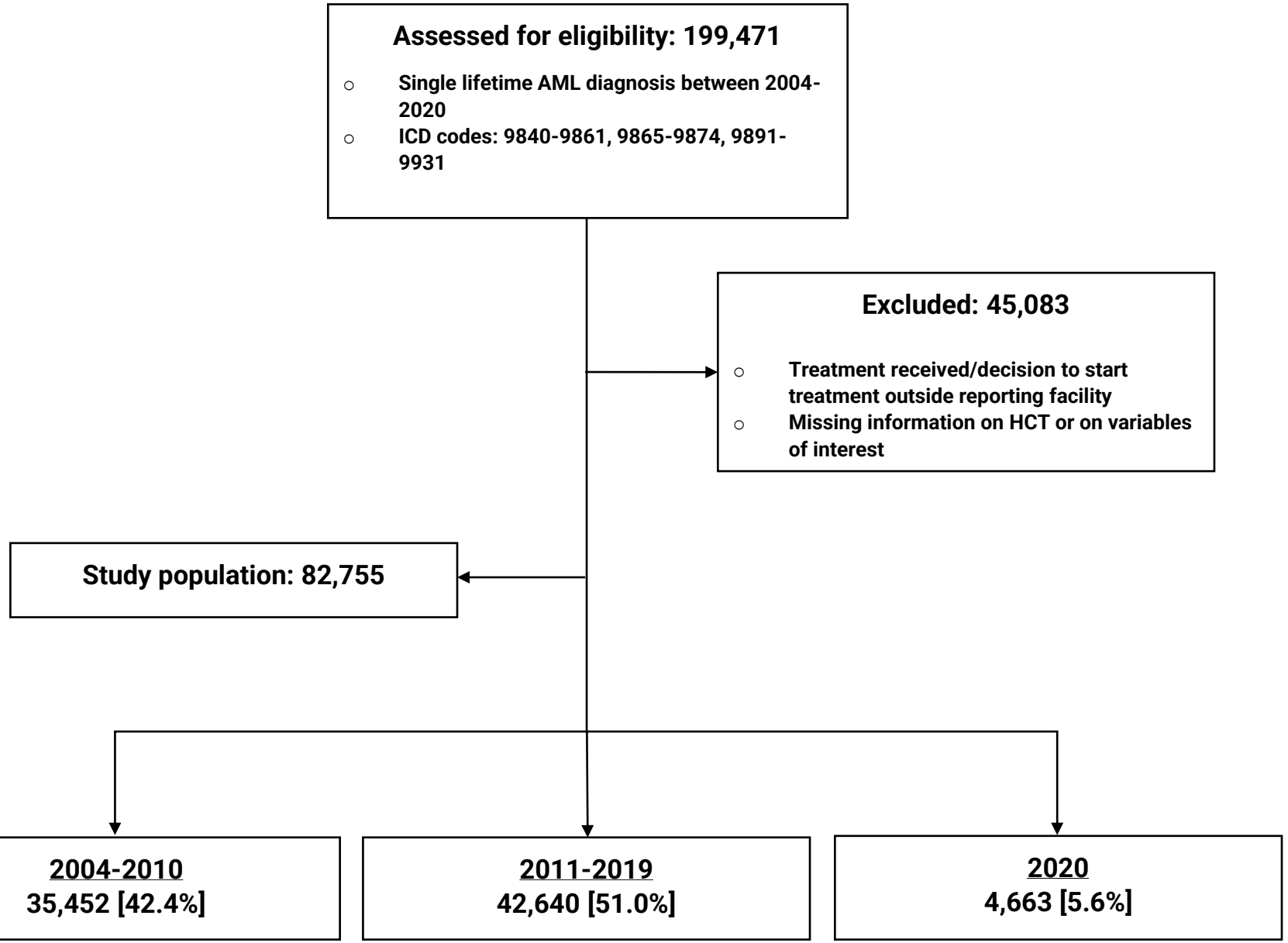


Pidala J, *et* al. Practice variation in physician referral for allogeneic hematopoietic cell transplantation

Methods

Study Characteristics

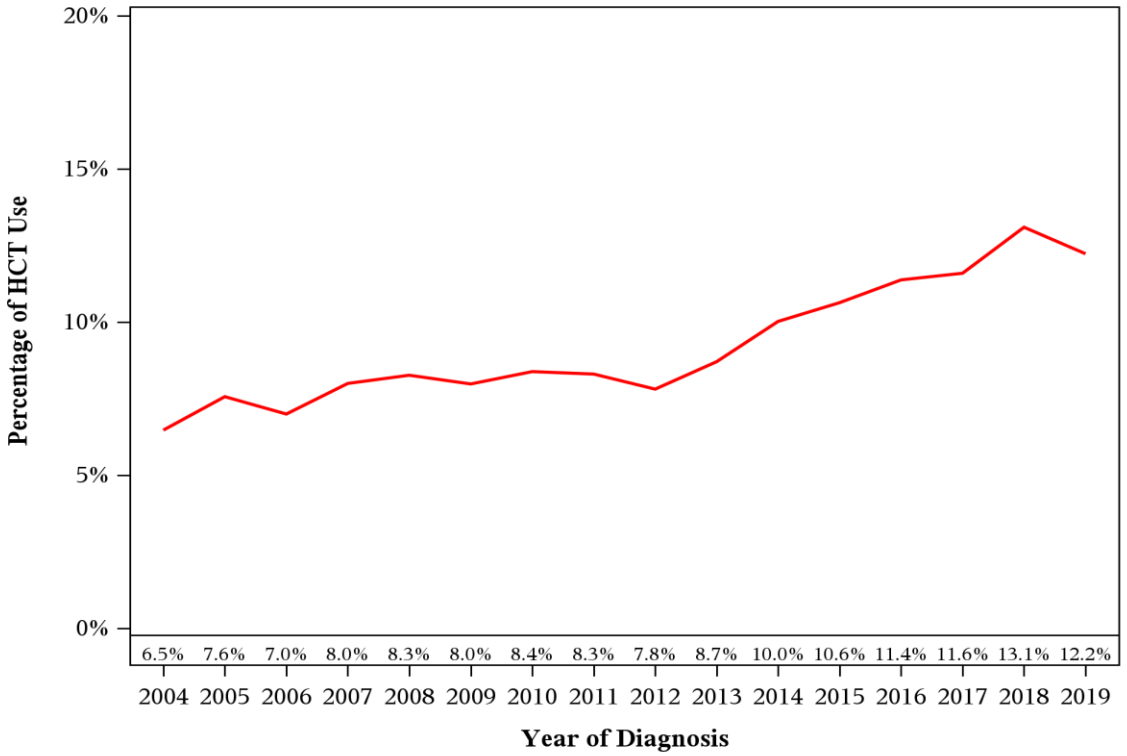
- Purpose: determine the effects of patient and disease characteristics on the odds of receiving HCT in AML
  - Retrospective analysis using data from the National Cancer Database (NCDB)
- Analyzed cohorts based on date of AML diagnosis:
  - 2004-2010
  - 2011-2019
  - 2020 (isolate the confounding effects of COVID-19 on HCT utilization)
- Statistical considerations
  - Logistic regression analysis
  - All statistical testing was two-sided and assessed for significance at the 5% level using SAS v9.4 (SAS Institute, Cary, NC)


Assessed for eligibility: 199,471
Single lifetime AML diagnosis between 2004-2020
ICD codes: 9840-9861, 9865-9874, 9891-9931
Excluded: 45,083
Treatment received/decision to start treatment outside reporting facility
Missing information on HCT or on variables of interest
Study population: 82,755
2004-2010
35,452 [42.4%]
2011-2019
42,640 [51.0%]
2020
4,663 [5.6%]

Results

HCT Use Over Time

- Out of 82,755 patients with AML, 7,764 (9.3%) received HCT
- HCT use increased from 2004-2020
  - 2004: 6.5%
  - 2019: 12.2%
  - 2020: 12%
- From 2011-2019, patients had 42% increased odds of receiving an HCT compared to 2004-2010
  - OR: 1.42 (95% CI: 1.35-1.49)



Age

- HCT use in AML declined with increasing age:
  - 18-40 years: 17.4%
  - 41-59 years: 16.4%
  - 60-70 years: 10%
  - 71-80 years: 1.5%

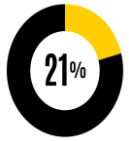
- The 18-40 age group had 47% higher odds of receiving HCT when compared to the 60-70 age group
  - OR: 0.53 (95% CI: 0.50-0.57)

- Elderly patients were more likely to receive HCT in 2011-2019 vs 2004-2010

Patient Characteristics 2004-2019		Odds ratio (95% CI)	p
Age & Year of Diagnosis	41-59 vs 18-40 / 2004-2010	0.79 (0.71-0.87)	p < 0.01
	41-59 vs 18-40 / 2011-2019	0.73 (0.67-0.80)	
	41-59 vs 60-70 / 2004-2010	2.67 (2.38-3.00)	
	41-59 vs 60-70 / 2011-2019	1.36 (1.25-1.47)	
	41-59 vs 71-80 / 2004-2010	31.65 (22.07-45.39)	
	41-59 vs 71-80 / 2011-2019	7.43 (6.40-8.63)	
	60-70 vs 18-40 / 2004-2010	0.29 (0.26-0.34)	
	60-70 vs 18-40 / 2011-2019	0.54 (0.49-0.59)	
	60-70 vs 71-80 / 2004-2010	11.85 (8.21-17.09)	
	60-70 vs 71-80 / 2011-2019	5.48 (4.73-6.35)	
	71-80 vs 18-40 / 2004-2010	0.02 (0.02-0.04)	
	71-80 vs 18-40 / 2011-2019	0.10 (0.08-0.11)	

IOWA

Age

Age	2004-2010	2011-2019	2020
18-40			
41-59			
60-70			
71-80			

Patient Characteristics 2020		Odds ratio (95% CI)	p
Age & Year of Diagnosis	41-59	0.89 (0.68-1.68)	p < 0.01
	60-70	0.62 (0.46-0.83)	
	71-80	0.14 (0.09-0.21)	
	81+	0.01 (0.00-0.04)	
	18-40	Reference	

IOWA

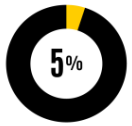
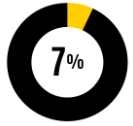
Comorbidities

- Higher Charlson-Deyo comorbidity indices (CCI) predicted lower rates of HCT use
  - 0: 11.0%
  - 1: 6.2%
  - 2-3: 3.3%
- Patients with a CCI of 0 had 66% increased odds of receiving HCT when compared to indices of 2-3
  - OR: 0.54 (95% CI: 0.50-0.58)
- Patients with higher CCIs were more likely to receive HCT in the 2011-2019 vs 2004-2010

Patient Characteristics 2004-2019		Odds ratio (95% CI)	p
Charlson-Deyo & Year of Diagnosis	1 vs 0 / 2004-2010	0.78 (0.69-0.89)	p = 0.03
	1 vs 0 / 2011-2019	0.71 (0.65-0.79)	
	1 vs 2-3 / 2004-2010	2.09 (1.55-2.80)	
	1 vs 2-3 / 2011-2019	1.33 (1.13-1.57)	
	2-3 vs 0 / 2004-2010	0.37 (0.28-0.49)	
	2-3 vs 0 / 2011-2019	0.54 (0.46-0.62)	

IOWA

Comorbidities

CCI	2004-2010	2011-2019	2020
0			
1			
2-3			

Patient Characteristics 2020		Odds ratio (95% CI)	p
Charlson-Deyo & Year of Diagnosis	1	0.63 (0.47-0.84)	p = 0.03
	2-3	0.57 (0.40-0.82)	
	0	Reference	

IOWA

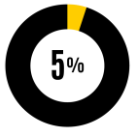
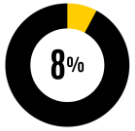
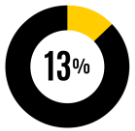
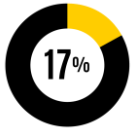
Distance to Treatment Centers

- Patients that received an HCT typically had longer travel distances to their treatment centers:
  - 0-4.9 miles: 4.4%
  - 5-11.9 miles: 6.7%
  - 12-34.7 miles: 11%
  - 34.8+ miles: 14.1%
- Patients that traveled 34.8+ miles had significantly greater odds of receiving HCT than patients that live 0-4.9 miles from treatment centers
  - OR: 3.57 (95% CI: 3.29-3.87)
- The odds of receiving HCT increased in patients that live closer to treatment centers in 2011-2019 vs 2004-2010

Patient Characteristics 2004-2019		Odds ratio (95% CI)	p
Distance & Year of Diagnosis	5-11.9 miles vs 0-4.9 miles / 2004-2010	1.10 (0.94-1.28)	p < 0.01
	5-11.9 miles vs 0-4.9 miles / 2011-2019	1.22 (1.08-1.38)	
	5-11.9 miles vs 12-34.7 miles / 2004-2010	0.60 (0.53-0.68)	
	5-11.9 miles vs 12-34.7 miles / 2011-2019	0.73 (0.67-0.81)	
	5-11.9 miles vs 34.8+ miles / 2004-2010	0.35 (0.31-0.40)	
	5-11.9 miles vs 34.8+ miles / 2011-2019	0.53 (0.48-0.58)	
	12-34.7 miles vs 0-4.9 miles / 2004-2010	1.82 (1.58-2.10)	
	12-34.7 miles vs 0-4.9 miles / 2011-2019	1.66 (1.49-1.87)	
	34.8+ miles vs 0-4.9 miles / 2004-2010	3.13 (2.72-3.59)	
	34.8+ miles vs 0-4.9 miles / 2011-2019	2.32 (2.07-2.59)	

IOWA

Distance to Treatment Centers

Distance	2004-2010	2011-2019	2020
0-4.9 miles			
5-11.9 miles			
12-34.7 miles			
34.8+ miles			

Patient Characteristics 2020		Odds ratio (95% CI)	p
Distance & Year of Diagnosis	5-11.9 miles	1.29 (0.88-1.89)	p = 0.03
	12-34.7 miles	1.73 (1.21-2.48)	
	34.8+ miles	2.40 (1.69-3.39)	
	0-4.9 miles	Reference	

IOWA

Race, Educational Status, Income and Primary Payor

Patient Characteristics 2004-2019		Odds ratio (95% CI)	p
Race	Black	0.60 (0.54-0.67)	p < 0.01
	Other	0.91 (0.81-1.02)	
	White	Reference	
Percent of Missing High School Education	14-19.9%	0.77 (0.72-0.83)	p < 0.01
	20-28.9%	0.68 (0.63-0.74)	
	>= 29%	0.64 (0.58-0.71)	
	< 14%	Reference	
Median Annual Income	$30,000-$34,999	1.09 (0.98-1.22)	p < 0.01
	$35,000-$45,999	1.30 (1.16-1.45)	
	>= $46,000	1.51 (1.34-1.70)	
	< $30,000	Reference	
Primary Payor	Not insured	0.35 (0.29-0.43)	p < 0.01
	Private	1.74 (1.63-1.85)	
	Public	Reference	

These trends did not significantly change in 2011-2019 vs 2004-2010

IOWA

Race, Educational Status, Income and Primary Payor

Patient Characteristics 2020		Odds ratio (95% CI)	p
Race	Black	0.81 (0.57-1.14)	p = 0.02
	Other	0.58 (0.81-1.02)	
	White	Reference	
Percent of Missing High School Education	5-9%	0.59 (0.44-0.78)	p < 0.01
	9.1-15.2%	0.55 (0.40-0.75)	
	>=15.3%	0.47 (0.33-0.68)	
	<5%	Reference	
Primary Payor	Not insured	0.40 (0.19-0.85)	p < 0.01
	Private	1.87 (1.51-2.32)	
	Public	Reference	

Median annual income was not correlated with odds of receiving HCT in the 2020 cohort

IOWA

AML Subtype

- Therapy-related AML had the highest rates of HCT
  - Overall study population: 12.8%
  - 2004-2010: 13.5%
  - 2011-2019: 12.1%
  - 2020: 20%
- Patients with acute promyelocytic leukemia had the lowest HCT rates
  - Overall study population: 0.4%
  - 2004-2010: 0.4%
  - 2011-2019: 0.3%
  - 2020: 0.5%
- The odds of receiving HCT did not significantly change in any AML subtype in 2011-2019 vs 2004-2010

AML Subtypes		Odds ratio (95% CI)	p-value
2004-2019	Acute Promyelocytic Leukemia	0.02 (0.01-0.03)	p < 0.01
	Core Binding Factor AML	0.48 (0.41-0.55)	
	Therapy-related AML	1.18 (0.81-1.71)	
	Other AML	Reference	
2020	Acute Promyelocytic Leukemia	0.02 (0.00-0.07)	p < 0.01
	Core Binding Factor AML	0.53 (0.35-0.82)	
	Therapy-related AML	1.52 (0.52-1.46)	
	Other AML	Reference	

IOWA

Discussion

The Positives

- To our knowledge, this is the largest scale analysis on HCT utilization in AML

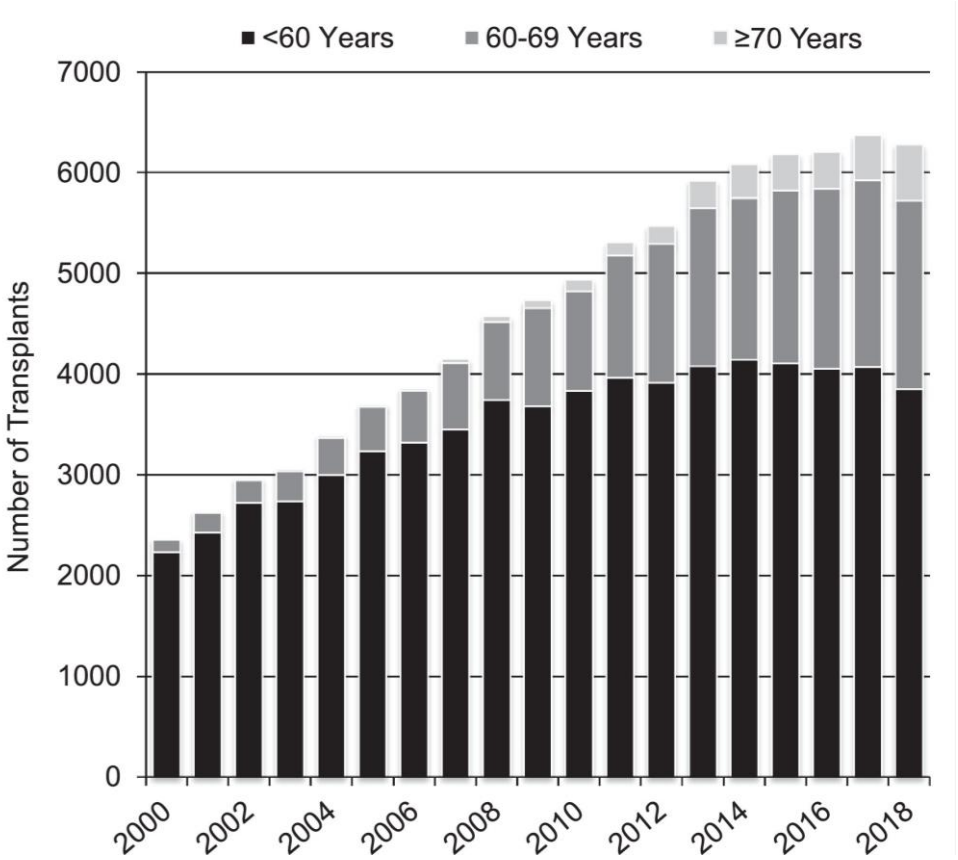
- The increase in HCT rates from 2004-2020, especially among elderly patients with multiple co-morbidities, may be due to improvements in:
  - Indication models based on molecular techniques
  - Better supportive care and management of complications (graft-versus-host disease)
  - Better donor availability (haploidentical donors)
  - Reduced-intensity conditioning regimens

Room for Improvement

- The persistent disparities in HCT rates with respect to economic status and race represent areas warranting further improvement
  - HCT continues to have high direct and indirect (transportation, temporary housing, travel distance) costs
    - There are few studies looking at improving cost-effectiveness of HCT
  - Varying out-of-pocket costs for insurances that offer coverage for HCT [6]
  - Racial differences in HLA-typing can contribute to disparities in donor availability[7]

Similar Studies

- D'Souza *et al* (2020)
  - Retrospective analysis of 2018 CIBMTR data on all disease types with HCT indications
  - Found increased rates of HCT utilization (allogenic and autologous) primarily among patients >70 years old
  - Also found diminished HCT rates among black patients
    - Interestingly, the use of haploidentical donors has improved allogenic HCT rates in minorities
      - 21% of HCT involving black patients have haploidentical donors compared to 4.6% from other unrelated donors



Similar Studies

- Tokaz *et al* (2022)
  - Retrospective analysis of Worldwide Network for Blood & Bone Marrow Transplantation data on AML (2009-2016)
  - Rates of HCT in AML continue to increase globally across all age groups
  - Despite this, economic disparities are still predictive of HCT utilization even in resource poor countries

Acknowledgements

- Contributing Authors:
  - Dr. Prajwal Dhakal
  - Bradley Loeffler
  - Dr. Ustav Joshi
  - Dr. Uttam Bhetuwal
  - Dr. Shiwani Sharma
  - Dr. Vijaya Raj Bhatt
  - Avantika Pyakuryal
- Holden Comprehensive Cancer Center
- ASCO Conquer Cancer Foundation

IOWA

References

1. Granot, *et al*. History of hematopoietic cell transplantation: Challenges and progress. Haematologica. 10.3324/haematol.2019.245688.
2. Pidala J, *et* al. Practice variation in physician referral for allogeneic hematopoietic cell transplantation. Bone Marrow Transplant. 2013 Jan;48(1):63-7.
3. Döhner H, *et al*. Diagnosis and management of AML in adults: 2022 recommendations from an international expert panel on behalf of the ELN. Blood. 2022 Sep 22;140(12):1345-1377
4. Snowden JA *et al*. European Society for Blood and Marrow Transplantation (EBMT). Indications for haematopoietic cell transplantation for haematological diseases, solid tumours and immune disorders: current practice in Europe, 2022. Bone Marrow Transplant. 2022 Aug;57(8):1217-1239
5. Esther N. Oliva, *et al*. The Real-World Incidence of Relapse in Acute Myeloid Leukemia (AML): A Systematic Literature Review (SLR). *Blood* 2018; 132 (Supplement 1): 5188
6. Preussler JM, *et al*. Costs and cost-effectiveness of hematopoietic cell transplantation. Biol Blood Marrow Transplant. 2012 Nov;18(11):1620-8
7. D'Souza A, *et al*. Current Use of and Trends in Hematopoietic Cell Transplantation in the United States. Biol Blood Marrow Transplant. 2020 Aug;26(8):e177-e182. Muffly L, et al.: Increasing use of allogeneic hematopoietic cell transplantation in patients aged 70 years and older in the United States. *Blood* 130:1156–1164, 2017
8. Tokaz MC, *et al*. An Analysis of the Worldwide Utilization of Hematopoietic Stem Cell Transplantation for Acute Myeloid Leukemia. Transplant Cell Ther. 2023 Apr;29(4):279.e1-279.e10.

IOWA

Questions?

Thank you