Not for publication or presentation

A G E N D A
CIBMTR WORKING COMMITTEE FOR HEALTH SERVICES AND INTERNATIONAL STUDIES
Orlando, FL
Friday, February 17, 2023, 12:00 p.m. – 2:00 p.m. (EST)

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1. Introduction

a. **Minutes from February 2022 meeting** (Attachment 1)
b. **Instructions for sign-in and voting**

2. Accrual Summary (Attachment 2)

3. Presentations, Published or Submitted Papers

a. **HS16-03** Karen K. Ballen, Tao Wang, Naya He, Shahrukh Hashmi, Leslie E. Lehmann, William A. Wood, Hemalatha G. Rangarajan, Wael Saber. Does Race/Ethnicity Impact Umbilical Cord Blood Transplant Outcomes in a Contemporary Era? ***Oral presentation, ASH 2022.***

b. **HS18-01** Yasuyuki Arai, Yoshiko Atsuta, Ruta Brazauskas, Naya He, Shahrukh Hashmi, Leslie E. Lehmann, William A. Wood, Hemalatha G. Rangarajan, Shingo Yano, Shinichi Kako, Masamitsu Yanada, Yukiyasu Ozawa, Noriko Doki, Yoshinobu Kanda, Takahiro Fukuda, Yuta Katayama, Tatsuo Ichinohe[18], Junji Tanaka, Junya Kanda, Takanori Teshima, Shinichiro Okamoto, Wael Saber; International Collaborative Study to Compare the Prognosis for Acute Leukemia Patients Transplanted with Intensified Myeloablative Regimens. ***Poster presentation, ASH 2022.***

c. **HS16-01** Trends in Utilization and Outcomes of Autologous and Allogeneic Hematopoietic cell Transplantation in Racial and Ethnic Minorities (N Khera/ T Hahn/ S Ailawadhi / W Saber) ***Poster Presentation, 2023 Tandem Meetings.***

d. **HS16-03** Relationship of Race/Ethnicity and Survival after Single and Double Umbilical Cord Blood Transplantation (K Ballen) ***Poster Presentation, 2023 Tandem Meetings.***

4. Studies in Progress (Attachment 3)

a. **HS16-01** Trends in Utilization and Outcomes of Autologous and Allogeneic Hematopoietic cell Transplantation in Racial and Ethnic Minorities (N Khera/ T Hahn/ S Ailawadhi / W Saber) **Manuscript Preparation.**

b. **HS16-03** Relationship of Race/Ethnicity and Survival after Single and Double Umbilical Cord Blood Transplantation (K Ballen) **Manuscript Preparation.**

c. **HS18-01** International collaborative study to compare the prognosis for acute leukemia patients transplanted with intensified myeloablative regimens (Y Arai/ Y Atsuta/ S Yano) **Manuscript Preparation.**

d. **HS18-02** Racial differences in long term survivor outcomes after allogeneic transplants (B Blue/ N Majhail) **Manuscript Preparation.**

e. **HS19-01** Factors Associated with Clinical Trial Participation among HCT Patients: A CIBMTR Analysis (T F. Gray/ A El-Jawahri) **Protocol Development.**

f. **HS19-03** Haploidentical Stem Cell Transplantation for malignant and non-malignant hematological diseases in patients without sibling donor: A multicenter prospective and longitudinal study of the Brazilian bone marrow transplantation study group (SBTMO) (N Hamerschlak/ M N Kerbauy/ A A F Ribeiro) **Data Collection.**

h. **HS19-04** Outcomes after allogeneic stem cell transplants performed in Brazil from HLA-matched siblings, unrelated and mismatched related donors. Retrospective study on behalf of the Brazilian Bone Marrow Transplantation Society (SBTMO), GEDECo (Brazil-Seattle Transplant-related complications Consortium), Hospital Israelita Albert Einstein (AmigoH), Associação da Medula Óssea do Estado de São Paulo (Ameo), Programa Nacional de Apoio à Atenção Oncológica (Pronon), and CIBMTR (A Seber/ N Hamerschlak/ M E Flowers/ M Pasquini) **Analysis**

i. **HS20-01** Resource Intensity of End-of-Life Care in Children After Hematopoietic Stem Cell Transplant for Acute Leukemia: Rates and Disparities **(**E E Johnston/ C W. Elgarten/ L Winestone/ R Aplenc/ K Getz/ V Huang/ Y Li) **Datafile Preparation.**

5. Future/Proposed Studies

a. **PROP 2209-20** Impact of Ambient Air Pollution Exposure on Outcomes in Pediatric Bone Marrow Transplantation (Paul George; Staci Arnold) (Attachment 4)

b. **PROP 2210-93** Community health status and long-term outcomes in 1-year survivors of autologous and allogeneic hematopoietic cell transplantation in the United States (Betty Hamilton; Sanghee Hong) (Attachment 5)

Proposed Studies; not accepted for consideration at this time

a. **PROP 2210-85** Outcomes of allogeneic hematopoietic stem cell transplantation based on access to care. *Dropped-low scientific impact.*

b. **PROP 2210-162** Socioeconomic Disparities Impacting Access to BCMA directed Chimeric Antigen Receptor T cell therapy and Clinical Outcomes. *Dropped-supplemental data needed.*

c. **PROP 2210-258** Geographic and Racial Disparities in Access to Chimeric Antigen Receptor-T Cells and Bispecific Antibodies. *Dropped-low scientific impact.*

6. Study Presentation

a. HS16-01 Analysis result update (N Khera)

b. Updates on the HS19-01 study (T Gray)

7. Future/proposed studies to be presented at the CIBMTR Collaborative Working Committee Study Proposals Session

a. **PROP 2210-172** Outcomes of Hispanic Adolescents and Young Adults (AYA) with Acute Lymphoblastic Leukemia After Allogeneic Stem Cell Transplant (Arjun Datt Law; Tommy Alfaro Moya) (Attachment 6) [*presentation at Collaborative Study Proposals Session*]

b. **PROP 2210-132, 2210-134, 2210-222, 2209-18** Characterizing differences in the clinical outcomes of commercial CAR T-cells for B-cell lymphoma, ALL, and multiple myeloma based on race/ ethnicity, sex, and socioeconomic status (O Montaner; J Norrell; W Fingrut; G Shah; S hong; E Umyarova; N Epperla) (Attachment 7) [*presentation at Collaborative Study Proposals Session*]

MINUTES AND OVERVIEW PLAN
CIBMTR WORKING COMMITTEE FOR HEALTH SERVICES AND INTERNATIONAL STUDIES
Salt Lake City, UT
Saturday, April 23, 2022, 12:15 – 1:45 PM MDT

Co-Chair:	**Shahrukh K. Hashmi, MD, MPH, Mayo Clinic;**
	Telephone: 507-284-3417; E-mail: hashmi.shahrukh@mayo.edu
Co-Chair:	**Leslie Lehmann, MD, Dana Farber Cancer Institute, Boston, MA;**
	Telephone: 617-632-4882; Email: leslie_lehmann@dfci.harvard.edu
Co-Chair:	**William A. Wood, MD, MPH, University of North Carolina, Chapel Hill, NC;**
	Telephone: 919-843-6517; E-mail: william_wood@med.unc.edu
Scientific Director:	**Wael Saber, MD, MS, CIBMTR Statistical Center;**
	Telephone: 414-805-0677; Email: wsaber@mcw.edu
Statistical Director:	**Ruta Brazauskas, PhD, CIBMTR Statistical Center;**
	Telephone: 414-955-8687; E-mail: ruta@mcw.edu
Statistician:	**Jinalben Patel, BDS, MPH, CIBMTR Statistical Center;**
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1. Introduction

a. *Minutes and Overview Plan from April 2022 meeting (Attachment 1)*

b. *Instructions for sign-in and voting*

The meeting was called to order at 1:15 pm by Dr. Shahrukh K. Hashmi. He announced leadership changes welcoming Hemalatha Rangarajan as incoming chair and William Wood as outgoing chair. He described the COI, Working Committees Membership, goals, expectations, and limitations of the committee, and he gave an introduction of the data that are collected in CRF and TED database, sources of cellular therapy data. He also explained the voting process, the role of working committee members, the rules of authorship, and the new collaborative study proposals session. He describes the two abstracts selected at ASH, HS16-01, and HS18-02 as clinically important papers and were already presented at ASH 2021. He encouraged audiences to submit proposals at TCT 2023, also for international research.

Dr. Wael Saber then gratified Naya for her work and welcomed Jinal as a new statistician.

2. Accrual summary (Attachment 2)

Due to the full agenda, the accrual summary of registration and research cases between 2008 and 2018 were not presented to the committee but were available as part of the Working Committee attachments.

3. Presentations, published or submitted papers

The progress of the ongoing studies during the past year were presented.

a. **HS16-01:** Trends in Volume and Outcomes of Autologous and Allogeneic Hematopoietic Cell Transplantation in Racial/Ethnic Minorities (Nandita Khera)**. *Analysis.***

b. **SC21-02:** Impact of Center Specific Analysis (CSA) on HCT Center Volumes (Akshay Sharma/Brent Logan/Leslie E Lehmann/ Hemalatha G Rangarajan/ Jaime Preussler/ Jesse D Troy/ Luke P Akard/ Neel S Bhatt/ Tony H Truong/ Willliam A Wood/ W Saber)**. Manuscript preparation.**

4. **Studies in progress** (Attachment 3)

a. **HS16-01:** Trends in Utilization and Outcomes of Autologous and Allogeneic Hematopoietic cell Transplantation in Racial and Ethnic Minorities (N Khera/ T Hahn/ S Ailawadhi / W Saber). ***Analysis.***

b. **HS16-03** Relationship of Race/Ethnicity and Survival after Single and Double Umbilical Cord Blood Transplantation (K Ballen). ***Analysis.***

c. **HS18-01:** International collaborative study to compare the prognosis for acute leukemia patients transplanted with intensified myeloablative regimens (Y Arai/ Y Atsuta/ S Yano). ***Analysis.***

d. **HS18-02:** Racial differences in long term survivor outcomes after allogeneic transplants (B Blue/ N Majhail). ***Manuscript preparation.***

e. **HS18-03:** Racial/ethnic disparities in receipt of hematopoietic cell transplantation and subsequent resource utilization in children with acute leukemia.

f. **HS19-01:** Factors Associated with Clinical Trial Participation among HCT Patients: A CIBMTR Analysis (T F. Gray/ A El-Jawahri). ***Data file preparation.***

g. **HS19-03:** Haploidentical Stem Cell Transplantation for malignant and non-malignant hematological diseases in patients without sibling donor: A multicenter prospective and longitudinal study of the Brazilian bone marrow transplantation study group (SBTMO)(N Hamerschlak/ M N Kerbauy/ A A F Ribeiro). ***Data collection.***

h. **HS19-04:** Outcomes after allogeneic stem cell transplants performed in Brazil from HLA-matched siblings, unrelated and mismatched related donors. Retrospective study on behalf of the Brazilian Bone Marrow Transplantation Society (SBTMO), GEDECo (Brazil-Seattle Transplant-related complications Consortium), Hospital Israelita Albert Einstein (AmigoH), Associação da Medula Óssea do Estado de São Paulo (Ameo), Programa Nacional de Apoio à Atenção Oncológica (Pronon), and CIBMTR (A Seber/ N Hamerschlak/ M E Flowers/ M Pasquini). ***Data file preparation.***

i. **HS20-01:** Resource Intensity of End-of-Life Care in Children After Hematopoietic Stem Cell Transplant for Acute Leukemia: Rates and Disparities **(**E E Johnston/ C W. Elgarten/ L Winestone/R Aplenc/ K Getz/ V Huang/ Y Li). **Protocol development.**

5. Future/proposed studies

Dr. Leslie Lehmann and Dr. William A. Wood led this section.

a. **PROP 2109-18:** Health Care Utilization and costs of haploidentical allogeneic stem cell transplants in a contemporary cohort of pediatric patients with acute leukemia and myelodysplastic syndrome. (Hema Rangarajan/ Prakash Satwani) (Attachment 4)

Dr. Rangarajan presented this study. The specific aims of this study are two-fold: 1. Determine cost & HCU associated with HaploHCT (PTCY +_ Ex-vivo) for pediatric patients (<=21 years) with acute leukemia (ALL, AML) and MDS from 2010-2020. 2. Compare costs & HCU HaploHCT with that of MSD, MUD, MMURD and UCB. If feasible compare costs & HCU: T replete (PTCY) vs T deplete (Ex-Vivo) approaches. Comments received on the inclusion criteria and how much proportion would be in PHIS. Dr. Rangarajan said that she would like to add data after 2019 and added that all the centers were in PHIS as its PHIS restricted and it would be US based. One participant asked if the cost before transplant is available in PHIS. Dr. Rangarajan replied these data were not available. A brief explanation of what is PHIS by Dr. Rangarajan. Graft equitation as a limitation of the study stated by Dr. Rangarajan.

b. **PROP 2110-28:** Utilization of chimeric antigen receptor (CAR) T-cells differs by race and ethnicity compared to autologous hematopoietic cell transplant (autoHCT) for NHL (Megan Herr/ Christine Ho/ Theresa Hahn) (Attachment 5)

Dr. Herr presented this study. The specific aims of this study are two folds: 1. Compare the proportion of race and ethnicity for first autoHCT vs first CAR T. 2. Describe therapy choices after a failed autologous HCT for NHL by race and ethnicity (including 2nd autoHCT, 1st allHCT, CAR T-cell, other, and no therapy). Comment received on restriction of population selection to the centers that perform the procedure and Dr. Herr responded that it would be restricted and also mentioned about considering the factor, how this patient is being treated as insurance coverage (Medicare, Medicaid). Study would focus only on US or US vs other country as sensitive analysis. Enough power considering the small sample size. One of the meeting participants noted concern that if the CIBMTR best database to answer the question and Dr. Herr said it is the best as CIBMTR have access to CAR-T follow up data.

c. **PROP 2110-164:** Changes in international Hematopoietic Cell Transplantation (HCT) Practices since publication of "Choosing Wisely BMT". (Matthew Seftel /Sita Bhella) (Attachment 6)

Dr. Seftel presented this study. The specific aims of this study are three-fold: 1. To measure BM vs. PBSC for MUD HCT after MA conditioning in pts with hematological malignancies. 2. To measure BM vs. PBSC for HCT in pts with aplastic anemia. 3. To measure Single vs. Double cord blood units for cord blood transplantation (CBT). Comments received on the definition on number of cord blood as adequate dose. Dr. Seftel said they are looking for cell doses reported in the data to decide if it was chosen wisely or not and added that size of cord blood availability should not be changed in pre and post years. One of the meeting participants noted concern that confounding factors can be center effect, covid. Dr. Seftel said to overcome the effect we would select the population broadly and considering covid impact there would data for 2 calendar years or do a sensitivity analysis to see drop after March.

d. **PROP 2110-229:** The Impact of Ethnicity, Race, and Socio-Economic Status (SES) in Mismatched Unrelated Donor (MMUD) Allogeneic Hematopoietic Cell Transplantation (HCT). (Trent Wang / Antonio Jimenez) (Attachment 7)

Dr. Wang presented this study. The specific aims of this study are three-fold: 1. To describe the racial/ethnic and SES composition of MMUD recipients. 2. To compare MMUD HCT outcomes among recipients of varying backgrounds in ethnicity/race and SES. 3. To evaluate the impact of GVHD prophylaxis regimes relative to ethnicity/race and SES. Comments were received on mismatched unrelated donor utilization has gone down significantly so if that would have impact on long term results of study. Meeting participants expressed concern regarding how much impact this study would have in future and if this is the right time to perform this study or wait for some time to get more data. One meeting participant suggested to breakdown race and ethnicity, Dr.Wang agreed.

e. **PROP 2110-31:** Characterizing differences in the clinical outcomes of and access to commercial CAR T-cells for relapsed/ refractory large B-cell lymphoma, based on patient race/ ethnicity, sex, and socioeconomic status

Dropped proposed studies

a. **PROP 2110-41:** Association of Racial and ethnic disparities and outcomes of acute leukemia patients receiving a haploidentical stem cell transplant. ***Dropped-overlap with recent study.***

b. **PROP 2110-140:** Trend in Survival in Patients Undergoing Allogeneic Hematopoietic Stem Cell Transplantation. ***Dropped overlap with recent study.***

c. **PROP 2110-226:** Comparing demographic characteristics of pediatric and young adult patients receiving cellular therapy versus hematopoietic stem cell transplantation for relapsed/refractory acute lymphoblastic leukemia. ***Dropped-low scientific impact.***

d. **PROP 2110-247:** Characterizing Changes in the Transplant and Cellular Therapy Workforce and Associations with Race-Ethnic Treatment Equity. ***Dropped-supplemental data needed.***

e. **PROP 2110-297:** Evaluation of Allogeneic Hematopoietic Cell Transplantation Outcomes in Underrepresented Minorities in the Era of Haploidentical Donor Transplant with Post-Transplant Cyclophosphamide. ***Dropped-overlap with recent study.***

6. CIBMTR strategic initiative: Fostering international collaboration

7. Other Business

Working Committee Overview Plan for 2022-2023

Study Number and Title	Current Status	Chairs Priority
HS16-01: Trends in utilization and outcomes of autologous and allogeneic hematopoietic cell transplantation in racial and ethnic minorities	Datafile preparation	2
HS16-03: Relationship of race/ethnicity and survival after single and double umbilical cord blood transplantation	Manuscript preparation	2
HS18-01: International collaborative study to compare the prognosis for acute leukemia patients transplanted with intensified myeloablative regimens	Manuscript preparation	2
HS18-02: Racial differences in long term survivor outcomes after Allogeneic hematopoietic cell transplantation	Manuscript preparation	2
HS18-03: Racial/ethnic disparities in receipt of hematopoietic cell transplantation and subsequent resource utilization in children with acute leukemia	Deferred	3
HS19-01: Factors associated with clinical trial participation among HSCT patients: a CIBMTR Analysis	Protocol Development	4
HS19-03: Haploidentical stem cell transplantation for malignant and non-malignant hematological diseases in patients without sibling donor: a multicenter prospective longitudinal study of the Brazilian bone marrow transplantation study group.	Data collection	4
HS19-04: Outcomes after allogeneic stem cell transplants performed in Brazil from HLA-matched siblings, unrelated and mismatched related donors. Retrospective study on behalf of the Brazilian Bone Marrow Transplantation Society (SBTMO), GEDECo (Brazil-Seattle)	Datafile preparation	4
HS20-01: Resource Intensity of end-of-life care in children after hematopoietic stem cell transplant for acute leukemia: Rates and disparities	Protocol pending	4

Working Assignments Assignments for Working Committee Leadership (May 2022)

Leslie Lehmann	**HS16-01:** Trends in utilization and outcomes of autologous and allogeneic hematopoietic cell transplantation in racial and ethnic minorities
	HS20-01: Resource Intensity of end-of-life care in children after hematopoietic stem cell transplant for acute leukemia: Rates and disparities
Hemalatha Rangarajan	**HS16-03:** Relationship of race/ethnicity and survival after single and double umbilical cord blood transplantation
	HS19-01: Factors associated with clinical trial participation among HSCT patients: a CIBMTR Analysis
Shahrukh Hashmi	**HS18-01:** International collaborative study to compare the prognosis for acute leukemia patients transplanted with intensified myeloablative regimens
	HS18-02: Racial differences in long term survivor outcomes after Allogeneic hematopoietic cell transplantation
	HS18-03: Racial/ethnic disparities in receipt of hematopoietic cell transplantation and subsequent resource utilization in children with acute leukemia
	HS19-03: Haploidentical stem cell transplantation for malignant and non-malignant hematological diseases in patients without sibling donor: a multicenter prospective longitudinal study of the Brazilian bone marrow transplantation study group
	HS19-04: Outcomes after allogeneic stem cell transplants performed in Brazil from HLA-matched siblings, unrelated and mismatched related donors. Retrospective study on behalf of the Brazilian Bone Marrow Transplantation Society (SBTMO), GEDECo (Brazil-Seattle)

Accrual Summary for the Health Services and International Studies Working Committee

Table 1. Characteristics of recipients who underwent a first allogeneic transplant registered with the CIBMTR

Characteristic	TED N (%)	CRF N (%)
No. of patients	255199	107880
No. of centers	651	576
Age at transplant, years - no. (%)		
Median (min-max)	37 (0-88)	33 (0-88)
0-9	35899 (14)	18296 (17)
10-19	32260 (13)	15735 (15)
20-29	33267 (13)	15215 (14)
30-39	36645 (14)	15975 (15)
40-49	41245 (16)	16128 (15)
50-59	40981 (16)	14013 (13)
60-69	29870 (12)	10446 (10)
70+	5032 (2)	2072 (2)
Recipient gender - no. (%)		
Male	149422 (59)	63370 (59)
Female	105777 (41)	44510 (41)
Recipient race - no. (%)		
Caucasian	171852 (67)	85200 (79)
African-American	12195 (5)	6468 (6)
Asian	18791 (7)	8427 (8)
Pacific islander	552 (0)	266 (0)
Native American	837 (0)	418 (0)
Other	8343 (3)	3927 (4)
Unknown	42629 (17)	3174 (3)
Disease - no. (%)		
Acute myelogenous leukemia	81398 (32)	30028 (28)
Acute lymphoblastic leukemia	43704 (17)	17627 (16)
Other leukemia	6209 (2)	2307 (2)
Chronic myelogenous leukemia	29293 (11)	14760 (14)
Myelodysplastic/myeloproliferative disorders	31820 (12)	14382 (13)
Other acute leukemia	2912 (1)	1020 (1)
Non-Hodgkin lymphoma	16894 (7)	6148 (6)
Hodgkin lymphoma	1624 (1)	630 (1)

Characteristic	TED N (%)	CRF N (%)
Plasma cell disorder/Multiple Myeloma	3279 (1)	1346 (1)
Other Malignancies	1178 (0)	500 (0)
Breast Cancer	179 (0)	90 (0)
Severe aplastic anemia	14472 (6)	7569 (7)
Inherited abnormalities erythrocyte differentiation or function	10504 (4)	5688 (5)
SCID and other immune system disorders	6520 (3)	3234 (3)
Inherited abnormalities of platelets	222 (0)	108 (0)
Inherited disorders of metabolism	2764 (1)	1557 (1)
Histiocytic disorders	1730 (1)	759 (1)
Autoimmune Diseases	136 (0)	47 (0)
Other diseases	361 (0)	80 (0)
Year of transplant - no. (%)		
<1985	4876 (2)	4486 (4)
1985-1989	10451 (4)	9326 (9)
1990-1994	22628 (9)	14566 (14)
1995-1999	35547 (14)	16563 (15)
2000-2004	40227 (16)	16777 (16)
2005-2009	39801 (16)	17647 (16)
2010-2014	46775 (18)	11102 (10)
2015-2019	48347 (19)	16291 (15)
2020-2021	6547 (3)	1122* (1)
Education - no. (%)	NA	
No primary education		64 (0)
Less than primary or elementary education		86 (0)
Primary of elementary education		724 (1)
Lower secondary education		798 (1)
Upper secondary education		11061 (10)
Post-secondary , non-tertiary education		4106 (4)
Tertiary education, Type A		8215 (8)
Tertiary education, Type B		1812 (2)
Advance research qualification		2157 (2)
Age<18 years old		31109 (29)
Missing		47748 (44)
Health insurance - no. (%)	NA	
No insurance		4321 (4)
Medicaid		9400 (9)

Characteristic	TED N (%)	CRF N (%)
Medicare		6248 (6)
Disability insurance		739 (1)
HMO		2434 (2)
Private health insurance		24879 (23)
National health insurance		15647 (15)
VA/Military		769 (1)
Other		3401 (3)
Missing		40042 (37)
Health insurance - no. (%)	NA	
No insurance		3441 (3)
Disability insurance +/-others		841 (1)
Private health insurance +/- others		30344 (28)
Medicaid +/-others		8303 (8)
Medicare +/-others		3836 (4)
Others		21073 (20)
Missing		40042 (37)
Occupation - no. (%)	NA	
Professional, technical, or related occupation		19220 (18)
Manager, administrator or proprietor		3916 (4)
Clerical or related occupation		2684 (2)
Sales occupation		2024 (2)
Service occupation		3287 (3)
Skilled crafts or related occupation		3242 (3)
Equipment/vehicle operator or related occupation		1504 (1)
Laborer		2097 (2)
Farmer		402 (0)
Member of military		338 (0)
Homemaker		1520 (1)
Student		10974 (10)
Under school age		2562 (2)
Not previously employed		2004 (2)
Other, specify		7874 (7)
Missing		44232 (41)

Footnote: * 2020 patients are not completed in current retrieval and no 2021 patients for CRF are included.

Table 2. Characteristics of recipients who underwent a first autologous transplant registered with the CIBMTR

Characteristic	TED N (%)	CRF N (%)
No. of patients	248578	46263
No. of centers	614	455
Age at transplant, years - no. (%)		
Median (min-max)	53 (0-86)	50 (0-83)
0-9	10825 (4)	2311 (5)
10-19	7802 (3)	1763 (4)
20-29	16577 (7)	3187 (7)
30-39	25099 (10)	5698 (12)
40-49	44346 (18)	9965 (22)
50-59	67513 (27)	12178 (26)
60-69	62524 (25)	9487 (21)
70+	13892 (6)	1674 (4)
Recipient gender - no. (%)		
Male	134801 (54)	22885 (49)
Female	113777 (46)	23378 (51)
Recipient race - no. (%)		
Caucasian	172878 (70)	36157 (78)
African-American	22073 (9)	5763 (12)
Asian	6308 (3)	1381 (3)
Pacific islander	331 (0)	56 (0)
Native American	750 (0)	222 (0)
Other	5401 (2)	1406 (3)
Unknown	40837 (16)	1278 (3)
Disease - no. (%)		
Acute myelogenous leukemia	8188 (3)	2398 (5)
Acute lymphoblastic leukemia	1625 (1)	474 (1)
Other leukemia	798 (0)	256 (1)
Chronic myelogenous leukemia	701 (0)	290 (1)
Myelodysplastic/myeloproliferative disorders	280 (0)	94 (0)
Other acute leukemia	150 (0)	31 (0)
Non-Hodgkin lymphoma	68209 (27)	11125 (24)
Hodgkin lymphoma	25504 (10)	4067 (9)
Plasma cell disorder/Multiple Myeloma	99848 (40)	15674 (34)

Characteristic	TED N (%)	CRF N (%)
Other Malignancies	19962 (8)	4337 (9)
Breast Cancer	21744 (9)	7295 (16)
Autoimmune Diseases	1038 (0)	136 (0)
Other diseases	531 (0)	86 (0)
Year of transplant - no. (%)		
<1985	31 (0)	5 (0)
1985-1989	2066 (1)	672 (1)
1990-1994	19307 (8)	7240 (16)
1995-1999	40356 (16)	12510 (27)
2000-2004	35076 (14)	6057 (13)
2005-2009	37167 (15)	7630 (16)
2010-2014	50043 (20)	4014 (9)
2015-2019	56464 (23)	7875 (17)
2020-2021	8068 (3)	260* (1)
Education - no. (%)	NA	
No primary education		18 (0)
Less than primary or elementary education		51 (0)
Primary of elementary education		341 (1)
Lower secondary education		398 (1)
Upper secondary education		6647 (14)
Post-secondary , non-tertiary education		2746 (6)
Tertiary education, Type A		5512 (12)
Tertiary education, Type B		1235 (3)
Advance research qualification		1714 (4)
Age<18 years old		3629 (8)
Missing		23972 (52)
Health insurance - no. (%)	NA	
No insurance		814 (2)
Medicaid		3643 (8)
Medicare		4484 (10)
Missing		37322 (81)
Health insurance - no. (%)	NA	
No insurance		814 (2)
Medicaid +/-others		3643 (8)
Medicare +/-others		4484 (10)
Missing		37322 (81)

Characteristic	TED N (%)	CRF N (%)
Occupation - no. (%)	NA	
Professional, technical, or related occupation		16632 (36)
Manager, administrator or proprietor		1818 (4)
Clerical or related occupation		1290 (3)
Sales occupation		862 (2)
Service occupation		1696 (4)
Skilled crafts or related occupation		1542 (3)
Equipment/vehicle operator or related occupation		857 (2)
Laborer		1027 (2)
Farmer		223 (0)
Member of military		166 (0)
Homemaker		644 (1)
Student		1140 (2)
Under school age		370 (1)
Not previously employed		1022 (2)
Other, specify		3430 (7)
Missing		13544 (29)

Footnote: *: * 2020 patients are not completed in current retrieval and no 2021 patients for CRF are included.

Table 3. Characteristics of recipients who received a first transplant from US centers reported to the CIBMTR, 2008 – 2019 (CRF)

Characteristic	Allogeneic N (%)	Autologous N (%)
No. of patients	28573	14129
No. of centers	184	180
Age at transplant, years - no. (%)		
Median (min-max)	51 (0-88)	58 (0-82)
0-9	3719 (13)	552 (4)
10-19	2414 (8)	255 (2)
20-29	2215 (8)	580 (4)
30-39	2190 (8)	801 (6)
40-49	3285 (11)	1818 (13)
50-59	5724 (20)	3993 (28)
60-69	7304 (26)	4980 (35)
70+	1722 (6)	1150 (8)
Recipient gender - no. (%)		
Male	16678 (58)	8159 (58)
Female	11895 (42)	5970 (42)

Characteristic	Allogeneic N (%)	Autologous N (%)
Recipient race - no. (%)		
Caucasian	22617 (79)	9659 (68)
African-American	3185 (11)	3416 (24)
Asian	1449 (5)	566 (4)
Pacific islander	99 (0)	34 (0)
Native American	195 (1)	118 (1)
Unknown	1028 (4)	336 (2)
Disease - no. (%)		
Acute myelogenous leukemia	9413 (33)	155 (1)
Acute lymphoblastic leukemia	3608 (13)	16 (0)
Other leukemia	756 (3)	14 (0)
Chronic myelogenous leukemia	757 (3)	0 (0)
Myelodysplastic/myeloproliferative disorders	7593 (27)	2 (0)
Other acute leukemia	277 (1)	2 (0)
Non-Hodgkin lymphoma	1690 (6)	3233 (23)
Hodgkin lymphoma	158 (1)	1144 (8)
Plasma cell disorder/Multiple Myeloma	167 (1)	8656 (61)
Other Malignancies	22 (0)	816 (6)
Breast Cancer	0 (0)	2 (0)
Severe aplastic anemia	1270 (4)	1 (0)
Inherited abnormalities erythrocyte differentiation or function	1173 (4)	7 (0)
SCID and other immune system disorders	984 (3)	44 (0)
Inherited abnormalities of platelets	35 (0)	0 (0)
Inherited disorders of metabolism	393 (1)	2 (0)
Histiocytic disorders	233 (1)	2 (0)
Autoimmune Diseases	18 (0)	29 (0)
Other diseases	26 (0)	4 (0)
Education - no. (%)		
No primary education	30 (0)	13 (0)
Less than primary or elementary education	53 (0)	27 (0)
Primary of elementary education	110 (0)	83 (1)
Lower secondary education	522 (2)	323 (2)
Upper secondary education	5785 (20)	3493 (25)
Post-secondary , non-tertiary education	1887 (7)	1189 (8)
Tertiary education, Type A	5397 (19)	2950 (21)
Tertiary education, Type B	1256 (4)	864 (6)
Advance research qualification	1016 (4)	556 (4)
Age<18 years old	5708 (20)	748 (5)
Missing	6809 (24)	3883 (27)

Characteristic	Allogeneic N (%)	Autologous N (%)
Health insurance - no. (%)		
No insurance	459 (2)	145 (1)
Medicaid	5777 (20)	1930 (14)
Medicare	5097 (18)	3085 (22)
Disability insurance	576 (2)	0 (0)
Private health insurance	14902 (52)	0 (0)
National health insurance	160 (1)	0 (0)
VA/Military	362 (1)	0 (0)
Other	520 (2)	0 (0)
Missing	720 (3)	8969 (63)
Health insurance - no. (%)		
No insurance	338 (1)	145 (1)
Disability insurance +/-others	631 (2)	0 (0)
Private health insurance +/- others	17747 (62)	0 (0)
Medicaid +/-others	5033 (18)	1930 (14)
Medicare +/-others	3057 (11)	3085 (22)
Others	1047 (4)	0 (0)
Missing	720 (3)	8969 (63)
Occupation - no. (%)		
Professional, technical, or related occupation	5677 (20)	3245 (23)
Manager, administrator or proprietor	2514 (9)	1384 (10)
Clerical or related occupation	1570 (5)	962 (7)
Sales occupation	1239 (4)	631 (4)
Service occupation	2060 (7)	1312 (9)
Skilled crafts or related occupation	1966 (7)	1116 (8)
Equipment/vehicle operator or related occupation	946 (3)	649 (5)
Laborer	1233 (4)	736 (5)
Farmer	205 (1)	139 (1)
Member of military	214 (1)	133 (1)
Homemaker	655 (2)	343 (2)
Student	4786 (17)	559 (4)
Under school age	1396 (5)	292 (2)
Not previously employed	623 (2)	375 (3)
Other, specify	1321 (5)	690 (5)
Missing	2168 (8)	1563 (11)
Recipient zip code - no. (%)		
Not Available	1958 (7)	786 (6)
Available	26615 (93)	13343 (94)

Table 4. Characteristics of recipients who received allogeneic transplants registered with the CIBMTR by WHO region, 2008 – 2021(TED)

Characteristic	Africa	Latin Americas	US / Canada	Eastern Mediterranean	Europe	Southeastern Asia	Western Pacific
No. of patients	37	5737	95086	4619	13942	2428	6262
No. of centers	2	53	215	16	111	15	27
Age, in years - no. (%)							
<10	0 (0)	1109 (19)	9781 (10)	1967 (43)	1146 (8)	817 (34)	943 (15)
10-19	6 (16)	1109 (19)	8029 (8)	1033 (22)	985 (7)	588 (24)	713 (11)
20-29	6 (16)	845 (15)	7931 (8)	777 (17)	1378 (10)	345 (14)	564 (9)
30-39	2 (5)	860 (15)	8171 (9)	448 (10)	1470 (11)	309 (13)	611 (10)
40-49	8 (22)	749 (13)	11849 (12)	245 (5)	2270 (16)	210 (9)	944 (15)
50-59	9 (24)	670 (12)	20485 (22)	114 (2)	3172 (23)	140 (6)	1363 (22)
60-69	6 (16)	329 (6)	23516 (25)	34 (1)	3070 (22)	19 (1)	1052 (17)
>=70	0 (0)	66 (1)	5324 (6)	1 (0)	451 (3)	0 (0)	72 (1)
Gender - no. (%)							
Male	27 (73)	3377 (59)	54887 (58)	2724 (59)	8213 (59)	1581 (65)	3657 (58)
Female	10 (27)	2360 (41)	40199 (42)	1895 (41)	5729 (41)	847 (35)	2605 (42)
Primary disease - no. (%)							
Acute myelogenous leukemia	13 (35)	1588 (28)	36750 (39)	807 (17)	5671 (41)	451 (19)	2465 (39)
Acute lymphoblastic leukemia	2 (5)	1518 (26)	15048 (16)	720 (16)	2117 (15)	299 (12)	1195 (19)
Chronic myelogenous leukemia	3 (8)	375 (7)	3070 (3)	130 (3)	492 (4)	82 (3)	187 (3)
Myelodysplastic disorders	7 (19)	677 (12)	17805 (19)	161 (3)	2653 (19)	172 (7)	1008 (16)
Non-Hodgkin lymphoma	3 (8)	136 (2)	6690 (7)	37 (1)	718 (5)	44 (2)	370 (6)
Hodgkin lymphoma	0 (0)	45 (1)	482 (1)	16 (0)	84 (1)	16 (1)	31 (0)
Multiple myeloma	1 (3)	4 (0)	305 (0)	10 (0)	73 (1)	1 (0)	7 (0)
Other malignancies	1 (3)	142 (2)	4015 (4)	59 (1)	716 (5)	23 (1)	280 (4)
Severe aplastic anemia	4 (11)	659 (11)	3548 (4)	520 (11)	513 (4)	330 (14)	250 (4)

Characteristic	Africa	Latin Americas	US / Canada	Eastern Mediterranean	Europe	Southeastern Asia	Western Pacific
Other non-malignancies	3 (8)	593 (10)	7373 (8)	2159 (47)	905 (6)	1010 (42)	469 (7)
Donor type - no. (%)							
HLA-identical sibling	16 (43)	2754 (48)	27075 (28)	3474 (75)	4642 (33)	1481 (61)	2220 (35)
Other Related donor	1 (3)	1252 (22)	13284 (14)	756 (16)	951 (7)	654 (27)	694 (11)
Unrelated donor	20 (54)	1730 (30)	54711 (58)	389 (8)	8348 (60)	293 (12)	3348 (53)
Missing	0 (0)	1 (0)	16 (0)	0 (0)	1 (0)	0 (0)	0 (0)
Graft type - no. (%)							
Bone Marrow	1 (3)	2951 (51)	20938 (22)	2522 (55)	2954 (21)	438 (18)	1023 (16)
Peripheral Blood	35 (95)	2607 (45)	66019 (69)	1758 (38)	10477 (75)	1988 (82)	4622 (74)
Cord Blood	1 (3)	175 (3)	8081 (8)	280 (6)	505 (4)	1 (0)	613 (10)
Missing	0 (0)	4 (0)	48 (0)	59 (1)	6 (0)	1 (0)	4 (0)
Year of transplant - no. (%)							
2008	5 (14)	159 (3)	4722 (5)	362 (8)	1486 (11)	13 (1)	275 (4)
2009	11 (30)	290 (5)	5350 (6)	414 (9)	1564 (11)	45 (2)	293 (5)
2010	8 (22)	376 (7)	5579 (6)	452 (10)	1571 (11)	33 (1)	367 (6)
2011	10 (27)	335 (6)	6118 (6)	221 (5)	1490 (11)	125 (5)	399 (6)
2012	1 (3)	398 (7)	6236 (7)	242 (5)	1497 (11)	144 (6)	458 (7)
2013	2 (5)	349 (6)	6717 (7)	221 (5)	1263 (9)	125 (5)	435 (7)
2014	0 (0)	375 (7)	6880 (7)	275 (6)	794 (6)	151 (6)	469 (7)
2015	0 (0)	353 (6)	7073 (7)	256 (6)	709 (5)	188 (8)	466 (7)
2016	0 (0)	335 (6)	7256 (8)	237 (5)	760 (5)	247 (10)	559 (9)
2017	0 (0)	393 (7)	7549 (8)	286 (6)	1402 (10)	288 (12)	475 (8)
2018	0 (0)	577 (10)	7950 (8)	372 (8)	517 (4)	311 (13)	481 (8)
2019	0 (0)	664 (12)	8192 (9)	439 (10)	387 (3)	327 (13)	513 (8)
2020	0 (0)	551 (10)	7558 (8)	335 (7)	282 (2)	189 (8)	503 (8)
2021	0 (0)	582 (10)	7906 (8)	507 (11)	220 (2)	242 (10)	569 (9)

Table 5. Allogeneic transplant recipients and centers by country registered with the CIBMTR, 2008-2021(TED)

Regions	N	Centers
Africa		
South Africa	37	2
Americas		
USA	88735	199
Argentina	517	7
Brazil	4565	32
Canada	6351	22
Chile	17	2
Venezuela	49	2
Mexico	211	3
Uruguay	69	3
Peru	108	1
Columbia	201	3
Eastern Mediterranean		
Saudi Arabia	3125	8
Egypt	21	2
Iran	552	1
Kuwait	3	1
Pakistan	918	4
Europe		
Austria	87	2
Belgium	1226	7
Denmark	1283	1
United Kingdom	1950	17
Finland	393	2
France	1059	10

Regions	N	Centers
Germany	2303	17
Ireland	154	1
Israel	930	7
Italy	529	7
Netherlands	586	8
Norway	87	1
Poland	215	4
Portugal	131	2
Spain	562	9
Sweden	807	4
Switzerland	705	3
Russia	19	1
Turkey	424	3
Greece	3	1
Czech Republic	385	3
Slovak Republic	104	1
Southeastern Asia		
India	2407	14
Thailand	21	1
Western Pacific		
Australia	4238	17
New Zealand	1070	9
Taiwan	61	1
Hong Kong	38	1
Singapore	855	4

Table 6. Number of patients who received a first allogeneic transplant registered with the CIBMTR between 2008 and 2021 by country

	CRF		TED	
Country	Malignant disease	Non-malignant disease	Malignant disease	Non-malignant disease
Argentina	<100	<100	100-500	<100
Australia	501-999	100-500	>=1000	100-500
Belgium	<100	<100	>=1000	100-500
Brazil	100-500	100-500	>=1000	501-999
Canada	100-500	100-500	>=1000	501-999
Colombia	<100	<100	100-500	<100
Czech Republic	<100	<100	100-500	<100
Denmark	100-500	<100	501-999	100-500
Finland	NA	NA	100-500	<100
France	<100	<100	501-999	100-500
Germany	100-500	<100	>=1000	100-500
India	100-500	501-999	501-999	501-999
Iran	<100	<100	100-500	100-500
Ireland	<100	<100	100-500	<100
Israel	<100	<100	501-999	100-500
Italy	NA	NA	100-500	<100
Mexico	<100	<100	100-500	<100
Netherlands	<100	<100	100-500	<100
New Zealand	100-500	<100	501-999	<100
Pakistan	<100	100-500	100-500	100-500
Poland	<100	<100	100-500	<100
Saudi Arabia	100-500	501-999	>=1000	>=1000
Singapore	100-500	<100	501-999	<100
South Korea	100-500	<100	>=1000	100-500
Spain	<100	<100	100-500	<100

	CRF		TED	
Country	**Malignant disease**	**Non-malignant disease**	**Malignant disease**	**Non-malignant disease**
Sweden	<100	<100	501-999	100-500
Switzerland	<100	<100	501-999	<100
Turkey	<100	<100	100-500	<100
UK	100-500	100-500	>=1000	100-500
USA	>=1000	>=1000	>=1000	>=1000

Countries with <100 patients in both CRF and TED dataset are not included in this report.

Table 7. Number of patients who received a first autologous transplant registered to the CIBMTR between 2008 and 2021 by country

	CRF		TED	
Country	**Malignant disease**	**Non-malignant disease**	**Malignant disease**	**Non-malignant disease**
Argentina	100-500	NA	>=1000	<100
Australia	<100	<100	501-999	<100
Belgium	NA	NA	100-500	<100
Brazil	100-500	<100	>=1000	<100
Canada	100-500	<100	>=1000	100-500
Colombia	<100	NA	100-500	<100
Czech Republic	<100	NA	100-500	<100
Finland	NA	NA	100-500	NA
France	NA	NA	501-999	<100
Germany	<100	NA	501-999	<100
India	<100	NA	501-999	<100
Iran	<100	NA	100-500	NA
Israel	<100	<100	501-999	<100

	CRF		TED	
Country	**Malignant disease**	**Non-malignant disease**	**Malignant disease**	**Non-malignant disease**
Italy	NA	NA	501-999	<100
Mexico	<100	NA	<100	100-500
Netherlands	NA	NA	100-500	<100
New Zealand	<100	NA	100-500	NA
Pakistan	<100	<100	100-500	NA
Poland	NA	NA	100-500	<100
Russia	NA	NA	100-500	<100
Saudi Arabia	<100	NA	>=1000	<100
Singapore	100-500	<100	501-999	<100
South Korea	<100	NA	501-999	<100
Spain	<100	NA	100-500	<100
Switzerland	NA	NA	100-500	<100
Turkey	<100	NA	501-999	<100
UK	NA	NA	100-500	NA
USA	>=1000	100-500	>=1000	100-500
Uruguay	<100	NA	501-999	NA
Venezuela	<100	NA	100-500	NA

Countries with <100 patients in both CRF and TED dataset are not included in this report.

CIBMTR®
CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH

TO: Health Services and International Studies Working Committee Members

FROM: Wael Saber, MD, MS; Rafeek Yusuf, MBBS, PHD; Scientific Directors for Health Services and International Studies Working Committee

RE: Studies in Progress Summary

HS16-01 Trends in Utilization and Outcomes of Autologous and Allogeneic Hematopoietic Cell Transplantation in Racial and Ethnic Minorities (N Khera/ T Hahn/ S Ailawadhi / W Saber) This study will evaluate the trends in utilization and clinical outcomes of autologous and allogeneic HCT in patients of different race/ ethnicity utilizing data collected by the Center for International Blood and Marrow Transplant Research (CIBMTR). This study is in the manuscript preparation phase. The goal of this study is to have the manuscript submitted by June 2023.

HS16-03 Relationship of Race/Ethnicity and Survival after Single and Double Umbilical Cord Blood Transplantation (K Ballen) This study will compare overall and disease free survivals for White, Hispanic, Asian, and Black patients after single and double umbilical cord blood transplantation; and determine if survival for White, Hispanic, Asian, and Black patients is comparable if transplanted with units of similar cell dose and HLA match. This study is in the manuscript preparation phase. The goal of this study is to have the manuscript submitted by June 2023.

HS18-01 International collaborative study to compare the prognosis for acute leukemia patients transplanted with intensified myeloablative regimens (Y Arai/ Y Atsuta/ S Yano). The aims of this study are: 1) To determine whether intensified myeloablative regimens of AraC or VP16 added to CY/TBI can improve the clinical outcomes (overall survival; OS) in allo-HSCT for acute leukemia. 2) To confirm the prognostic differences (OS, non-relapse mortality, and relapse) between the conventional and intensified myeloablative regimens in each patient's characteristic such as age, comorbidity, disease risk/status, donor source, GVHD prophylaxis and so on. 3)To compare the OS, non-relapse mortality, and relapse of intensified regimen between the US and Japan. This study is in the manuscript preparation phase. The goal of this study is to have the manuscript submitted by June 2023.

HS18-02 Racial differences in long term survivor outcomes after allogeneic transplants (B Blue/ N Majhail) The aims of this study are: 1) To determine association of ethnicity/race and socioeconomic status (SES) on OS among adult allogeneic HCT recipients with hematologic malignancies who have survived for at least 1 year in remission. 2)To investigate the cumulative incidence of NRM and relapse post-transplant by ethnicity/race and SES in allogeneic HCT recipients who have survived in remission

for at least 1 year. 3)To compare standardized mortality ratio between our cohort of 1-year transplant survivors with that of their age- and gender-matched peers in general population (analyses will be stratified by ethnicity/race). This study is in the manuscript preparation phase. The goal of this study is to have the manuscript submitted by June 2023.

HS19-01 Factors Associated with Clinical Trial Participation among HCT Patients: A CIBMTR Analysis (T F. Gray/ A El-Jawahri) The primary aims of this study are: 1) To describe rates of clinical trial participation based on HCT type; 2) To explore factors that are associated with clinical trial participation in patients with undergoing HCT; 3) To assess the impact of clinical trial participation on overall survival (OS) and non-relapse mortality (NRM) in autologous and allogeneic HCT recipients. This study is in the protocol development phase.

HS19-03 Haploidentical Stem Cell Transplantation for malignant and non-malignant hematological diseases in patients without sibling donor: A multicenter prospective and longitudinal study of the Brazilian bone marrow transplantation study group (SBTMO) (N Hamerschlak/ M N Kerbauy/ A A F Ribeiro). The primary objective of this study is determine if the 1year Overall Survival after Hematopoietic Stem Cell Transplantation (HCT) plus post-Cy from Haploidentical related donor (Haplo – HCT) for acute myeloid leukemia, acute lymphoblastic leukemia and Myelodysplastic / myelo-proliferative disorders is not inferior compared to matched related or unrelated allogeneic HCT donor with 10/10 and 9/10 compatibility. This study is in the data collection phase.

HS19-04 Outcomes after allogeneic stem cell transplants performed in Brazil from HLA-matched siblings, unrelated and mismatched related donors. Retrospective study on behalf of the Brazilian Bone Marrow Transplantation Society (SBTMO), GEDECo (Brazil-Seattle Transplant-related complications Consortium), Hospital Israelita Albert Einstein (AmigoH), Associação da Medula Óssea do Estado de São Paulo (Ameo), Programa Nacional de Apoio à Atenção Oncológica (Pronon), and CIBMTR (A Seber/ N Hamerschlak/ M E Flowers/ M Pasquini). The primary objective of this study is to compare 1-year overall survival after allogeneic HCT performed in Brazil from URD, Haplo and MSD. The secondary objective of this study is to compare the 100-day transplant-related mortality (TRM) and the 1-year event-free survival (EFS) after allogeneic HCT performed in Brazil from URD, Haplo and MSD. This study is analysis phase.

HS20-01 Resource Intensity of End-of-Life Care in Children After Hematopoietic Stem Cell Transplant for Acute Leukemia: Rates and Disparities (E E Johnston/ C W. Elgarten/ L Winestone/ R Aplenc/ K Getz/ V Huang/ Y Li) The primary aims of this study are: 1) Describe the resource utilization during the 30 days before death among children who received a HSCT for a hematologic malignancy and then died within 5

years at the same PHIS hospital. 2) Determine the prevalence of patients with a resource intense phenotype in the last 30 days of life among children who received a HSCT for a hematologic malignancy and then died within 5 years at the same PHIS hospital. 3) Determine the clinical and sociodemographic characteristics associated with a resource intense phenotype among children who received a HSCT for a hematologic malignancy and then died within 5 years at the same PHIS hospital. This study is in the Datafile preparation phase.

Response Summary:

This form is intended to be completed by a physician/researcher for the purpose of proposing a study. Content should not include Personal Identifiable Information (PII) or Protected Health Information (PHI). If you are a patient, do not complete this form. Patients: Contact your healthcare provider immediately for reports of problems with your treatment or problems with products received for your treatment. The CIBMTR uses de-identified data and is unable to associate reported treatment problems, adverse events, or corrections of information with a center, clinical trial, or healthcare provider.

Q1. Study Title

Impact of Ambient Air Pollution Exposure on Outcomes in Pediatric Bone Marrow Transplantation

Q2. Key Words

Pollution, bone marrow transplant, hematopoietic cell transplantation, health services research

Q3. PRINCIPAL INVESTIGATOR

Provide the following information for each investigator:

Principal Investigator #1:

First and last name, degree(s):	Paul George, MD
Email address:	pegeorg@emory.edu
Institution name:	Emory University / Children's Healthcare of Atlanta
Academic rank:	Fellow in Pediatric Hematology/Oncology

Q4. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- Yes

Q5. Do you identify as an underrepresented/minority?

- No

Q6. Principal Investigator #2 (If applicable):

First and last name, degree(s):	Staci Arnold
Email address:	Staci.denise.arnold@emory.edu
Institution name:	Emory University / Children's Healthcare of Atlanta
Academic rank:	Associate Professor

Q7. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- No

Q8. Do you identify as an underrepresented/minority?

- Yes

Q9. We encourage a maximum of two Principal Investigators per study. If more than one author is listed, please indicate who will be identified as the corresponding PI below:

N/A

Q10. If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:

N/A

LETTER OF COMMITMENT:

Please note: *A letter of commitment will be signed by Lead and Last authors as it describes the expectations for filling that role. By signing the letter of commitment, the authors accept their responsibilities and will be held accountable for timely completion of all steps in the project. More details regarding author responsibilities can be found here:* *https://www.cibmtr.org/Studies/Observational/StudyManagement/p*

Q12. CURRENT ONGOING WORK WITH CIBMTR: Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.

none

Q13. PROPOSED WORKING COMMITTEE:

- Health Services and International Studies

Q14. Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.

- No

Q15. RESEARCH QUESTION:

It is well-established that sociodemographic factors, including neighborhood, race/ethnicity, and health insurance status, affect outcomes in pediatric hematology, oncology, and bone marrow transplant (BMT). However, the underlying biologic mechanisms through which these factors affect health outcomes remains unclear. Our research question is: Does ambient (outdoor) air pollution exposure, a well-documented risk factor in other disease settings, significantly impact overall survival and event free survival among pediatric BMT recipients?

Q16. RESEARCH HYPOTHESIS:

We hypothesize that ambient air pollution exposure is a key biologic link between sociodemographic risk factors and poor health outcomes and therefore higher levels of neighborhood air pollution will be associated with worse overall survival and event free survival among pediatric BMT recipients. We further hypothesize that these associations will be highest amongst socially-vulnerable patients, including those living in high-poverty neighborhoods, minority patients, and those without private insurance.

Q17. SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.)

Suggested word limit of 200 words:

a. Create a database that links BMT patient information with ambient air pollution exposure, using CIBMTR data for patient information and publicly-available NASA Socioeconomic Data and Applications Center (SEDAC) data for neighborhood air pollution (fine particulate matter, PM2.5) exposure.
b. Examine the relationship between ambient air pollution exposure and health outcomes, using the database described above. The primary exposure of interest will be neighborhood PM2.5 levels (continuous variable), and the primary outcomes of interest will be overall survival and event-free survival (binary variable). Covariates of interest will include: age, gender, race, ethnicity, disease (malignant vs. non-malignant), neighborhood poverty, primary insurance. Interactions between air pollution exposure and key sociodemographic factors will also be investigated as secondary outcomes, as we hypothesize that air pollution exposure has increased harms amongst patients living in poverty. Time-to-event analyses will also be performed as key secondary outcomes.

Q18. SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.

We will test the hypothesis that ambient air pollution exposure is a clinically significant risk factor for poor outcomes in pediatric BMT. To our knowledge, there have been no published studies that examine the impact of ambient air pollution on BMT outcomes, which represents a key gap in the literature given the morbidity caused by air pollution exposure in other health settings. If validated, our findings could be translated into targeted clinical interventions for the most high-risk BMT patients (e.g. pollution exposure assessments and avoidance strategies via mobile app-based messaging, reduction via air filtration) and support investigations of pollution's effects in other high-risk settings in BMT (e.g. adult BMT recipients, pediatric cellular therapy patients).

Q19. SCIENTIFIC JUSTIFICATION: Provide a background summary of previous related research and their strengths and weaknesses, justification of your research and why your research is still necessary.

Pollution is a major cause of death and disability and is especially harmful for those with underlying organ damage, including cardiovascular, cerebrovascular, kidney, and lung disease.1 Furthermore, morbidity due to ambient air pollution is most prevalent and severe among minorities and otherwise marginalized populations.2 Infants and young children are also especially sensitive to the effects of air pollution: they breathe more air per bodyweight than adults, their metabolic pathways are immature and unable to rapidly detoxify and/or excrete pollutants, and their developmental processes are delicate and easily disrupted.3 The most well-studied and potentially damaging air pollutant is fine particulate matter, especially those with a diameter of 2.5 microns or less (PM2.5), and no safe threshold of PM2.5 has been identified.4 Though the underlying pathophysiology of air pollution exposure is complex, three key systemic pathways have been identified which contribute to morbidity and mortality in humans: dysregulated inflammation, altered metabolic pathways, and endothelial damage.5,6 Notably, these same pathways contribute to transplant-related morbidity and mortality in pediatric BMT recipients.7,8 As such, there is a strong pathophysiologic basis to suspect that air pollution exposure could be especially harmful in pediatric BMT recipients.
Of note, I am currently a third-year fellow in pediatric hematology-oncology and a second year PhD student in Health Services Research. My primary fellowship project has involved characterizing the effects of air pollutant levels on outcomes in children with sickle cell disease, using the same PM2.5 database I propose to use for this project. To date, I have found that increases in daily air pollution levels are associated with increased emergency department utilization (data not yet published, manuscript in preparation) and I am currently expanding the analysis to include patient-level risk factors (hemoglobin type (e.g. HbSS vs HbSC), medication use, insurance, neighborhood poverty level) in addition to neighborhood pollution levels.

Q19a. SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF)

N/A

Q20. PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.

a. Inclusion Criteria
i. Pediatric patient (age <21 years) having undergone BMT in the contiguous United States
ii. BMT date Jan 1, 2001 – Jan 1, 2018
b. Exclusion Criteria
i. Home address unavailable or outside the contiguous United States
ii. Prior BMT, cellular therapy, or solid organ transplant

Q21. Does this study include pediatric patients?

- Yes

Q22. DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion-variables to be considered in the multivariate analyses. Data collection forms available at: http://www.cibmtr.org/DataManagement/DataCollectior Outline any supplementary data required. Additional data collection is extremely difficult and will make your proposal less feasible.

Of note, the data I am hoping to utilize seems to be quite similar to the dataset that Dr. Kira Bona and colleagues used for their analysis of neighborhood poverty and allogeneic hematopoietic cell transplantation outcomes, published in 2021.9 I propose to augment their analysis by adding neighborhood air pollution levels as the primary exposure of interest, with similar outcomes and covariates of interest as used in their analysis and described below. As such, I could potentially use/build on her dataset, including address and/or zip-code (preferably 9-digit).

a. Sociodemographic information

i. Date of birth, Sex, Ethnicity, Race, Home Address/Zip Code of Residence, Combined Household Income, Type of Insurance (Medicaid vs Private vs Other vs Uninsured), Number of people in household

b. Pre-transplant information

i. Disease/reason for BMT (primary diagnosis), pre-transplant Karnofsky/Lansky scale

c. Transplant

i. Donor (allo vs haplo vs auto), Product type (cord, peripheral blood, bone marrow), match/mismatch (number)

ii. Prep regimen (myeloablative, non-myeloablative, RIC), irradiation and field, date of transplant

d. Post-transplant course

i. Date of marrow recovery/engraftment

ii. GVDH

1. Did acute GVHD develop? (yes/no and maximum overall grade)

2. Did chronic GVHD develop? (yes/no and maximum overall grade)

a. Did pulmonary cGVHD develop?

iii. Did the recipient develop TMA? (yes/no)

iv. Did the recipient develop VOD/SOS? (yes/no)

v. Did the recipient develop a clinically significant infection? (yes/no, bacterial, viral, fungal)

vi. Did the recipient develop non-infectious lung complications, including: IPn (yes/no), ARDS (yes/no), COP (yes/no), BOOP (yes/no), DAH (yes/no)?

vii. Did the recipient develop a secondary malignancy (yes/no), myelodysplastic (yes/no), or proliferative syndrome (yes/no)?

1. Date

viii. Did the recipient experience graft failure? (yes/no)

1. Date

ix. Did the recipient's original disease relapse? (yes/no)

1. Date

x. Death? (yes/no)

1. Primary cause of death

2. Date

Q23. **PATIENT REPORTED OUTCOME (PRO) REQUIREMENTS: If the study requires PRO data collected by CIBMTR, the proposal should include: 1) A detailed description of the PRO domains, timepoints, and proposed analysis of PROs; 2) A description of the hypothesis specific to PROS.**

For additional information on what PRO measures have been collected and timepoints of collection, please reach out to the Late Effects and Quality of Life or Health Services Working Committee leadership: https://www.cibmtr.org/About/WhoWeAre/Com

N/a – patient reported outcomes not required

Q24. **SAMPLE REQUIREMENTS: If the study requires biologic samples from the CIBMTR Repository, the proposal should also include: 1) A detailed description of the proposed testing methodology and sample requirements; 2) A summary of the investigator's previous experience with the proposed assay systems. PIs should be encouraged to review the inventory details, sample types collected and reach out to research_repos@nmdp.org with any questions.**

More information can be found at: https://www.cibmtr.org/Samples/Inventory/Pages/index

N/a – biologic samples not required

Q25. NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required, i.e., neither database contains all the data required to answer the study question.

I will combine the CIBMTR data with air pollution data from a publically available national database developed by the NASA Socioeconomic Data and Applications Center (SEDAC).10 This database contains daily PM2.5 levels in 1km x 1km grids covering the contiguous United States from January 1, 2001 to Dec 31, 2018, which I am currently using for my fellowship project looking at the impact of air pollution on sickle cell disease outcomes. Remote-sensing and other SEDAC PM2.5 data have been well-validated and published in other health settings as well, such as evaluation of total mortality, cardiorespiratory disease, asthma, and cancers.11

I must account for the fact that, as Dr. Bona and colleagues have shown, socioeconomic status (SES) impacts both health outcomes and air pollution exposure. To do so, we will include SES as a confounding variable. To create this variable, we will use CDC/ATSDR Social Vulnerability Index (SVI) database (https://www.atsdr.cdc.gov/placeandhealth/svi/index.html). This publicly available database, created by the Centers for Disease Control and Prevention, uses United States Census data to estimate the social vulnerability of every census tract for a given year; our analysis will incorporate the SES theme and the housing/transportation theme.

Q26. REFERENCES:

1. Wang H, Naghavi M, Allen C, et al. Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980–2015: a systematic analysis for the Global Burden of Disease Study 2015. The Lancet. 2016;388(10053):1459-1544. doi:10.1016/S0140-6736(16)31012-1

2. Pratt GC, Vadali ML, Kvale DL, Ellickson KM. Traffic, Air Pollution, Minority and Socio-Economic Status: Addressing Inequities in Exposure and Risk. International Journal of Environmental Research and Public Health. 2015;12(5):5355-5372. doi:10.3390/ijerph120505355

3. Landrigan PJ, Fuller R, Fisher S, et al. Pollution and children's health. Science of The Total Environment. 2019;650:2389-2394. doi:10.1016/j.scitotenv.2018.09.375

4. Ambient (outdoor) air pollution. Accessed December 23, 2021. https://www.who.int/news-room/fact-sheets/detail/ambient-(outdoor)-air-quality-and-health

5. Anderson JO, Thundiyil JG, Stolbach A. Clearing the Air: A Review of the Effects of Particulate Matter Air Pollution on Human Health. J Med Toxicol. 2012;8(2):166-175. doi:10.1007/s13181-011-0203-1

6. Xie W, You J, Zhi C, Li L. The toxicity of ambient fine particulate matter (PM2.5) to vascular endothelial cells. Journal of Applied Toxicology. 2021;41(5):713-723. doi:10.1002/jat.4138

7. Hill GR. Inflammation and Bone Marrow Transplantation. Biology of Blood and Marrow Transplantation. 2009;15(1, Supplement):139-141. doi:10.1016/j.bbmt.2008.11.008

8. Palomo M, Diaz-Ricart M, Carbo C, et al. Endothelial Dysfunction after Hematopoietic Stem Cell Transplantation: Role of the Conditioning Regimen and the Type of Transplantation. Biology of Blood and Marrow Transplantation. 2010;16(7):985-993. doi:10.1016/j.bbmt.2010.02.008

9. Bona K, Brazauskas R, He N, et al. Neighborhood poverty and pediatric allogeneic hematopoietic cell transplantation outcomes: a CIBMTR analysis. Blood. 2021;137(4):556-568. doi:10.1182/blood.2020006252

10. Di Q, Wei Y, Shtein A, et al. Daily and Annual PM2.5 Concentrations for the Contiguous United States, 1-km Grids, v1 (2000 - 2016). Published online 2021. doi:10.7927/0RVR-4538

11. Li J, Lu X, Liu F, et al. Chronic Effects of High Fine Particulate Matter Exposure on Lung Cancer in China. Am J Respir Crit Care Med. Published online July 2, 2020. doi:10.1164/rccm.202001-0002OC

Q27. **CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning:**

1. Employment (such as an independent contractor, consultant or providing expert testimony)?
2. Relationships (such as executive and advisory committee positions, medical consultant, speaker's bureau)?
3. Ownership (such as equity, ownership or financial interests)?
4. Transactions (such as honoraria, patents, royalties and licenses)?
5. Legal (such as pending or current arbitration or legal proceedings)?

- No, I do not have any conflicts of interest pertinent to this proposal

Q27a. **If yes, provide detail on the nature of employment, name of organization, role, entity, ownership, type of financial transaction or legal proceeding and whether renumeration is >$5000 annually.**

N/A

BEFORE FINAL SUBMISSION, please review the PI checklist to ensure that you have completed all necessary steps. This will increase the likelihood of submitting a feasible and successful proposal.

Embedded Data:

N/A

RESEARCH QUESTION:
It is well-established that sociodemographic factors, including neighborhood, race/ethnicity, and health insurance status, affect outcomes in pediatric hematology, oncology, and bone marrow transplant (BMT). However, the underlying biologic mechanisms through which these factors affect health outcomes remains unclear. Our research question is: Does ambient (outdoor) air pollution exposure, a well-documented risk factor in other disease settings, significantly impact overall survival and event free survival among pediatric BMT recipients?

RESEARCH HYPOTHESIS:
We hypothesize that ambient air pollution exposure is a key biologic link between sociodemographic risk factors and poor health outcomes and therefore higher levels of neighborhood air pollution will be associated with worse overall survival and event free survival among pediatric BMT recipients. We further hypothesize that these associations will be highest amongst socially-vulnerable patients, including those living in high-poverty neighborhoods, minority patients, and those without private insurance.

Table 1: Characteristics of patients who received first allogeneic and autologous transplant, age less than 21 years from 2001 to 2017 registered with CIBMTR.

Characteristic	Allo-HCT	Auto-HCT	Total
No. of patients	10336	1229	11565
No. of centers	161	106	175
Recipient's age in years - no. (%)			
Median (min-max)	8 (0-20)	5 (-39-20)	8 (-39-20)
<5	3610 (35)	610 (50)	4220 (36)
5-10	2626 (25)	241 (20)	2867 (25)
11-15	2010 (19)	144 (12)	2154 (19)
16-<21	2090 (20)	234 (19)	2324 (20)
Sex - no. (%)			
Male	6185 (60)	682 (55)	6867 (59)
Female	4151 (40)	547 (45)	4698 (41)
Race - no. (%)			
White	7432 (72)	891 (72)	8323 (72)
Black or African American	1500 (15)	199 (16)	1699 (15)
Asian	488 (5)	59 (5)	547 (5)
Native Hawaiian or other Pacific Islander	31 (0)	3 (0)	34 (0)
American Indian or Alaska Native	101 (1)	8 (1)	109 (1)
Missing	784 (8)	69 (6)	853 (7)
Disease indication for Transplant, - no. (%)			
AML	2217 (21)	16 (1)	2233 (19)

Characteristic	Allo-HCT	Auto-HCT	Total
ALL	2364 (23)	2 (0)	2366 (20)
CLL	42 (0)	1 (0)	43 (0)
CML	269 (3)	0 (0)	269 (2)
MDS	616 (6)	1 (0)	617 (5)
Other acute leukemia	152 (1)	1 (0)	153 (1)
NHL	251 (2)	58 (5)	309 (3)
HD	104 (1)	137 (11)	241 (2)
PCD	3 (0)	2 (0)	5 (0)
ST	57 (1)	970 (79)	1027 (9)
SAA	866 (8)	1 (0)	867 (7)
Inherited abnormalities of erythrocyte differentiation	1072 (10)	0 (0)	1072 (9)
Disorders of the immune system	1190 (12)	32 (3)	1222 (11)
Inherited abnormalities of platelets	57 (1)	0 (0)	57 (0)
Inherited disorders of metabolism	630 (6)	1 (0)	631 (5)
Histiocytic disorders	372 (4)	0 (0)	372 (3)
Autoimmune disease	14 (0)	7 (1)	21 (0)
Other disease	41 (0)	0 (0)	41 (0)
Myeloproliferative Neoplasms	19 (0)	0 (0)	19 (0)
Graft Source - no. (%)			
Bone Marrow	4767 (46)	69 (6)	4836 (42)
Peripheral blood	1828 (18)	1156 (94)	2984 (26)
Cord blood	3729 (36)	4 (0)	3733 (32)
Missing	12 (0)	0 (0)	12 (0)
GVHD prophylaxis - no. (%)		NA	
No GVHD prophylaxis	146 (1)		
Ex-vivo T-cell depletion	621 (6)		
CD34 selection	357 (3)		
Post-CY + other(s)	214 (2)		
TAC + MMF +- other(s) (except post-CY)	1067 (10)		
TAC + MTX +- other(s) (except MMF, post-CY)	1805 (17)		
TAC + other(s) (except MMF, MTX, post-CY)	338 (3)		
TAC alone	144 (1)		
CSA + MMF +- other(s) (except post-CY)	1795 (17)		
CSA + MTX +- other(s) (except MMF, post-CY)	1996 (19)		
CSA + other(s) (except MMF, MTX, post-CY)	1167 (11)		
CSA alone	186 (2)		
Other(s)	119 (1)		
Missing	381 (4)		

Characteristic	Allo-HCT	Auto-HCT	Total
Conditioning regimen - no. (%)			
MAC	5970 (58)	690 (56)	6660 (58)
RIC/NST	1090 (11)	29 (2)	1119 (10)
Missing	3276 (32)	510 (41)	3786 (33)
Donor type - no. (%)		NA	
HLA-identical sibling	1702 (16)		
Twin	2 (0)		
Other related	681 (7)		
Well-matched unrelated (8/8)	2597 (25)		
Partially-matched unrelated (7/8)	1155 (11)		
Mis-matched unrelated (<= 6/8)	384 (4)		
Multi-donor	17 (0)		
Unrelated (matching TBD)	63 (1)		
Cord blood	3729 (36)		
Missing	6 (0)		
Time from diagnosis to transplant, months - no. (%)			
<3	1635 (16)	32 (3)	1667 (14)
3-5	2716 (26)	445 (36)	3161 (27)
6-8	1099 (11)	365 (30)	1464 (13)
9-11	619 (6)	102 (8)	721 (6)
>12	4267 (41)	285 (23)	4552 (39)
Zip code available - no. (%)			
No	1738 (17)	398 (32)	2136 (18)
Yes	8598 (83)	831 (68)	9429 (82)
Year of transplant- no. (%)			
2001	580 (6)	86 (7)	666 (6)
2002	585 (6)	55 (4)	640 (6)
2003	624 (6)	23 (2)	647 (6)
2004	673 (7)	55 (4)	728 (6)
2005	743 (7)	114 (9)	857 (7)
2006	793 (8)	89 (7)	882 (8)
2007	774 (7)	66 (5)	840 (7)
2008	777 (8)	199 (16)	976 (8)
2009	735 (7)	80 (7)	815 (7)
2010	472 (5)	12 (1)	484 (4)
2011	305 (3)	18 (1)	323 (3)
2012	326 (3)	28 (2)	354 (3)
2013	509 (5)	79 (6)	588 (5)

Characteristic	**Allo-HCT**	**Auto-HCT**	**Total**
2014	638 (6)	72 (6)	710 (6)
2015	689 (7)	96 (8)	785 (7)
2016	595 (6)	80 (7)	675 (6)
2017	518 (5)	77 (6)	595 (5)
Follow-up, months - median (range)	89 (1-246)	75 (0-236)	88 (0-246)

Table 2 – Availability of Zip codes for Allo patients

	Year of Transplant		
Zip code available	>=2013	<2013	Total
No	115 (4)	1623 (22)	1738
Yes	2834 (96)	5764 (78)	8598

Table 3 – Availability of Zip codes for Auto patients

	Year of Transplant		
Zip code available	>=2013	<2013	Total
No	18 (4)	380 (46)	398
Yes	386 (96)	445 (54)	831

Response Summary:

This form is intended to be completed by a physician/researcher for the purpose of proposing a study. Content should not include Personal Identifiable Information (PII) or Protected Health Information (PHI). If you are a patient, do not complete this form. Patients: Contact your healthcare provider immediately for reports of problems with your treatment or problems with products received for your treatment. The CIBMTR uses de-identified data and is unable to associate reported treatment problems, adverse events, or corrections of information with a center, clinical trial, or healthcare provider.

Q1. Study Title

Community health status and long-term outcomes in 1-year survivors of autologous and allogeneic hematopoietic cell transplantation in the United States

Q2. Key Words

hematopoietic cell transplantation, community health, allogeneic transplant, autologous transplant, long-term survival

Q3. PRINCIPAL INVESTIGATOR

Provide the following information for each investigator:

Principal Investigator #1:

First and last name, degree(s):	Betty Hamilton, MD, BS
Email address:	hamiltb2@ccf.org
Institution name:	Cleveland Clinic Taussig Cancer Center
Academic rank:	

Q4. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- No

Q5. Do you identify as an underrepresented/minority?

- No

Q6. Principal Investigator #2 (If applicable):

First and last name, degree(s):	Sanghee Hong, MD
Email address:	sanghee.hong@duke.edu
Institution name:	Duke University Medical Center
Academic rank:	Assistant Professor of Medicine

Q7. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- Yes

Q8. Do you identify as an underrepresented/minority?

- No

Q9. We encourage a maximum of two Principal Investigators per study. If more than one author is listed, please indicate who will be identified as the corresponding PI below:

Corresponding PI is Julia Joo (PI #1)
Additionally, we have been corresponding with a senior Principal Investigator, Dr. Betty Hamilton, MD (Associate staff, Cleveland Clinic, hamiltb2@ccf.org).

Q10. If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:

N/A

LETTER OF COMMITMENT:

Please note: *A letter of commitment will be signed by Lead and Last authors as it describes the expectations for filling that role. By signing the letter of commitment, the authors accept their responsibilities and will be held accountable for timely completion of all steps in the project. More details regarding author responsibilities can be found here:* *https://www.cibmtr.org/Studies/Observational/StudyManagement/p*

Q12. CURRENT ONGOING WORK WITH CIBMTR: Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.

None

Q13. PROPOSED WORKING COMMITTEE:

- Health Services and International Studies

Q14. Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.

- Yes

Q14a. If you have already spoken with a scientific director or working committee chair regarding this study, then please specify who:

Wael Saber, MD, MS

Q15. RESEARCH QUESTION:

Are community health factors associated with long-term outcomes for patients after autologous and allogeneic HCT?

Q16. RESEARCH HYPOTHESIS:

We hypothesize that poor community health factors (high community risk), measured using the County Health Rankings and Roadmaps (CHRR) database,(refs 1,2) are associated with inferior long-term outcomes in HCT recipients surviving at least 1 year after transplant.

Q17. SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.)

Suggested word limit of 200 words:

Primary:
Our primary aim is to investigate the association between community health status based on patient's residence (Patient Community Score [PCS]) and both continuous and 5-year overall survival (OS) in long-term survivors (≥1 year) of allogeneic and autologous HCT. The PCS will be generated using CHRR data associated with patient zip code/county to assess the overall health of the communities that patients return to after their transplant.
Secondary:
1. Investigate the association between PCS and the following long-term transplant outcomes: non-relapse mortality (NRM), relapse, and chronic graft-versus-host disease (cGVHD) (measured by incidence and maximum grade, only for allogeneic HCT recipients).
2. Investigate the association between PCS and other late effects of transplant (listed under "Transplant Outcomes and Late Effects" in Data Requirements section).
3. Identify associations between long-term outcomes (secondary aim 1) or late effects (secondary aim 2) and each of the four PCS subcategories: physical environment, social and economic factors, clinical care, and health behaviors.
Note: Allogeneic and autologous HCTs will be evaluated separately for both primary and secondary objectives, as applicable.

Q18. SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.

While many social determinants of health, such as race and income, have been identified to affect HCT outcomes, these individual factors cannot fully explain the complex health disparities surrounding HCT.(refs 3–5) Additionally, much of the literature in health disparities and HCT outcomes focus on the short-term period of recovery, generally within the first year or two of transplant.(refs 1,4,6) Many patients remain near their transplant centers for the first few months after transplant where they can be vigilantly monitored for complications. After moving back to their home community, however, transplant-related complications such as chronic GVHD, relapse, or other late effects may not be as well-recognized or cared for depending on the health resources in that community.(ref 7) A host of late complications across multiple organ systems can emerge years after HCT as a consequence of the intensive preconditioning for HCT or as a manifestation of cGVHD.(refs 7,8) Some of these complications, such as cardiac dysfunction due to pre-conditioning radiation exposure, are rare and can present sub-clinically, making the diagnosis of a late effect challenging at an under-resourced facility.(ref 7) Thus, the community health status of the patient's residence may play a significant role in their long-term outcomes.
Longer term survivors of transplant may continue to face health challenges after they move away from the close surveillance of their well-resourced transplant center, including low availability of clinical resources in the community, limiting access to care to their local primary care physicians, or physicians who are familiar with transplant-related care. Additionally, poor air/water quality and general health behaviors among community members (e.g. tobacco and substance use, poor diet and exercise habits) could also affect the overall health and wellness of HCT recipients and impede their continued recovery and wellness. Socioeconomic factors of the community (e.g. household income, community safety, family/social support) may also be major contributors to how HCT survivors are able to access resources longer term post-transplant. While studies have investigated some of these factors independently, few studies have considered all these factors comprehensively, thus missing the more complex, multifactorial effects that community health may have on recovery post-transplant. Understanding the specific community-level barriers to healthcare within these communities by evaluating the subcategories of the PCS score will further enable us to design targeted interventions and adjust follow-up care appropriately for these patients.

Q19. SCIENTIFIC JUSTIFICATION: Provide a background summary of previous related research and their strengths and weaknesses, justification of your research and why your research is still necessary.

Several studies have used the CHRR dataset (further detailed in the "Non-CIBMTR Data Source" section) to assess community health status in association with outcomes from solid organ transplants and cancer management.(refs 9–11) Poor community health was found to be associated with worse outcomes after kidney transplant as well as in endocrine cancer management.(refs 9,11) These studies only focused on solid cancers, however.

Three recent studies were conducted evaluating CHRR in HCT recipients. Hong et al. initially investigated CHRR in autologous and allogeneic transplant recipients at our single center. However, given the limitations of geographic representation of the majority of patients residing within the region, no significant association between CHRR and outcomes were found.(ref 12) A subsequent study led by Hong et al. using CIBMTR data with a nationally representative cohort of patients did demonstrate that poor community health status was associated with significantly higher overall mortality (HR 1.04 per PCS point, p = 0.0089) and non-relapse mortality (HR 1.08 per PCS point, p = 0.0004) in allogeneic HCT recipients.(ref 1) This study did not evaluate long-term outcomes, however, and did not investigate the effects after autologous HCT.

In this current proposal, we aim to further investigate the role of community health status in longer-term survivors of HCT in a nationally representative cohort in both autologous and allogeneic HCT recipients. We hypothesize that high community risk, measured by CHRR, is associated with inferior long-term outcomes in HCT recipients surviving at least 1 year after transplant. Joo et al. conducted a single center study evaluating the association between community health quality and outcomes in long-term (surviving ≥1 year) allogeneic and autologous transplant recipients (Figure 1B).(ref 13) The study was again noted to be limited by geographic representation of our cohort, which was predominantly in the northeast region of Ohio near our transplant center. We believe that a more nationally representative cohort will increase the range of Patient Community Scores (Figure 1C)(ref 1) and allow us to more accurately measure the association of community risk with long-term outcomes.

We thus propose to evaluate the impact of community risk as measured by the PCS using health factors of CHRR associated with zip code on long-term survival, NRM, and the late effects post-allogeneic HCT. Given their differences in long-term outcomes, autologous and allogeneic HCT recipients will be analyzed separately. In each group of HCT recipients, we will perform a Cox proportional hazards model to analyze associations of PCS and overall survival, non-relapse mortality and relapse. For the NRM and relapse analysis, cohort will be restricted to hematologic malignancies. Additional patient, sociodemographic, transplant and disease specific variables will be included. We will include patients who received HCT between the years 2015-2017, which should provide a large enough sample to sufficiently power our study and provide at least 6 years of follow-up data. Additionally, we will use the CHRR 2018 dataset to calculate the community risk, as this was previously used by the CIBMTR in Hong et al,(ref 1) and can also be used in this analysis to describe the communities to which patients return post-transplant.

Q19a. SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF)

[Click here]

Q20. PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.

Inclusion:
- Patients who received their first allogeneic or autologous HCT between 2015-2017
- Survived for at least 1 year after transplant
- Transplanted at a US center
- All disease, conditioning, donor and graft sources are included
- Age at least 18 years

Exclusion
- Patients whose primary disease relapsed or progressed <1 year post-HCT
- Patients who died <1 year post-HCT
- Missing zip code data

Q21. Does this study include pediatric patients?

- No

Q21a. If this study does not include pediatric patients, please provide justification:

The studies we have based our research question and hypothesis off of have focused on adult populations. Pediatric populations also have significantly different outcome risks after HCT than adult populations.

Q22. DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion-variables to be considered in the multivariate analyses. Data collection forms available at: http://www.cibmtr.org/DataManagement/DataCollectior Outline any supplementary data required. Additional data collection is extremely difficult and will make your proposal less feasible.

- Patient characteristics
o Age at transplant, by decade
o Sex: male versus female
o Race/ethnicity: Non-Hispanic white vs. Non-Hispanic black vs. Hispanic vs. Asian vs. Other
o Zip code of patient residence
o Median household income based on zip code
o Co-morbidity index (HCT-CI): 0 vs. 1-2 vs. 3+
o Karnofsky score prior to transplant: <80 vs. >80
o Employment: full time vs. part-time vs. unemployed vs medical disability
o Marital status: single vs married vs separated vs divorced vs widowed
o Distance between residence and transplant center (mi): <20 vs 20-50 vs 50-150 vs >150
- Disease characteristics
o Diagnosis
AML
MDS
MPN
ALL/other acute leukemias
NHL
HL
CML
Plasma cell neoplasm
Non-malignant conditions
Others
o Disease risk index
- Transplant Characteristics
o Year of transplant
o Type of transplant (auto or allo)
o Preparative regimen intensity: MA vs. RIC/NMA
o Use of TBI as a part of conditioning
o Donor: HLA-identical sibling vs. HLA-matched unrelated donor vs. mismatched unrelated donor, vs. umbilical cord blood
o Graft: peripheral blood, bone marrow, umbilical cord blood
o Recipient/donor CMV status
- Transplant Outcomes and Late Effects: continuous and at 5 years after HCT(refs 7,8)
o Acute GVHD: yes, no, grade
o Chronic GVHD : yes, no, grade
o Relapse: yes vs no, date of relapse
o Overall Survival
o Cause of death
o Subsequent new malignancy
o Avascular necrosis
o Congestive heart failure
o Diabetes mellitus
o Myocardial infarction
o Renal failure warranting dialysis
o Pneumonia syndrome
o Stroke
o Psychiatric (depression, anxiety)

Q23. **PATIENT REPORTED OUTCOME (PRO) REQUIREMENTS: If the study requires PRO data collected by CIBMTR, the proposal should include: 1) A detailed description of the PRO domains, timepoints, and proposed analysis of PROs; 2) A description of the hypothesis specific to PROS.**

For additional information on what PRO measures have been collected and timepoints of collection, please reach out to the Late Effects and Quality of Life or Health Services Working Committee leadership: https://www.cibmtr.org/About/WhoWeAre/Com

NA

Q24. **SAMPLE REQUIREMENTS: If the study requires biologic samples from the CIBMTR Repository, the proposal should also include: 1) A detailed description of the proposed testing methodology and sample requirements; 2) A summary of the investigator's previous experience with the proposed assay systems. PIs should be encouraged to review the inventory details, sample types collected and reach out to research_repos@nmdp.org with any questions.**

More information can be found at: https://www.cibmtr.org/Samples/Inventory/Pages/index

NA

Q25. NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required, i.e., neither database contains all the data required to answer the study question.

The County Health Rankings and Roadmaps (CHRR) is a program that provides publicly available data to build awareness of the multiple social factors that influence health. The CHRR uses a database of county-level factors to describe the health disparities of a community,(ref 2) including physical environment, social and economic factors, clinical care, and health behaviors. Data for the CHRR are compiled from several publicly available data sources.(ref 2) The score obtained from the CHRR model describing a community's health has been used to study outcomes of solid organ transplants and HCT.(refs 9,11,12)

We would generate a nationally standardized Patient Community Score (PCS) using the health factors of CHRR associated with the ZIP code of the patient residence.(refs 1,12) PCS would be calculated as the sum of weighted Z-scores of the 30 county-level community health factors considered in CHRR for 2018, which would allow us to assess patients with at least 5 years of follow-up onward (assuming we use CIBMTR 2023 data). We chose the 2018 database in part because the CIBMTR health services group has worked with this database before and will be familiar with how to use it for our analysis.(ref 1)

The health factors fall under 4 categories: health behavior (tobacco and alcohol use, diet and exercise, and high-risk sexual behavior), clinical care (access and quality of care), social and economic factors (education, employment, income, family and social support, and community safety), and physical environment (environmental quality and built environment). This kind of comprehensive and detailed community health data is not provided by CIBMTR datasets, but is critical to our study objectives in describing community health risks.

Q26. REFERENCES:

1. Hong S, Brazauskas R, Hebert KM, et al. Community health status and outcomes after allogeneic hematopoietic cell transplantation in the United States. Cancer 2021;127(4):609–18.
2. Remington PL, Catlin BB, Gennuso KP. The County Health Rankings: rationale and methods. Popul Health Metr 2015;13:11.
3. Fu S, Rybicki L, Abounader D, et al. Association of socioeconomic status with long-term outcomes in 1-year survivors of allogeneic hematopoietic cell transplantation. Bone Marrow Transplant 2015;50(10):1326–30.
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7. Majhail NS, Rizzo JD, Lee SJ, et al. Recommended screening and preventive practices for long-term survivors after hematopoietic cell transplantation. Biol Blood Marrow Transplant 2012;18(3):348–71.
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9. Schold JD, Buccini LD, Kattan MW, et al. The Association of Community Health Indicators With Outcomes for Kidney Transplant Recipients in the United States. Arch Surg 2012;147(6):520–6.
10. Schold J, Heaphy E, Buccini L, et al. Prominent Impact of Community Risk Factors on Kidney Transplant Candidate Processes and Outcomes. Am J Transplant 2013;13(9):10.1111/ajt.12349.
11. Al-Qurayshi Z, Randolph GW, Srivastav S, Kandil E. Outcomes in endocrine cancer surgery are affected by racial, economic, and healthcare system demographics. Laryngoscope 2016;126(3):775–81.
12. Hong S, Rybicki LA, Corrigan D, Schold JD, Majhail NS. Community Risk Score for Evaluating Health Care Disparities in Hematopoietic Cell Transplantation. Biol Blood Marrow Transplant 2018;24(4):877–9.
13. Joo JH, Hong S, Rybicki LA, Hamilton BK, Majhail NS. Community health status and long-term outcomes in 1-year survivors of autologous and allogeneic hematopoietic cell transplantation. Bone Marrow Transplant 2022;57(4):671–3.

Q27. **CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning:**

1. Employment (such as an independent contractor, consultant or providing expert testimony)?
2. Relationships (such as executive and advisory committee positions, medical consultant, speaker's bureau)?
3. Ownership (such as equity, ownership or financial interests)?
4. Transactions (such as honoraria, patents, royalties and licenses)?
5. Legal (such as pending or current arbitration or legal proceedings)?

- No, I do not have any conflicts of interest pertinent to this proposal

Q27a. **If yes, provide detail on the nature of employment, name of organization, role, entity, ownership, type of financial transaction or legal proceeding and whether renumeration is >$5000 annually.**

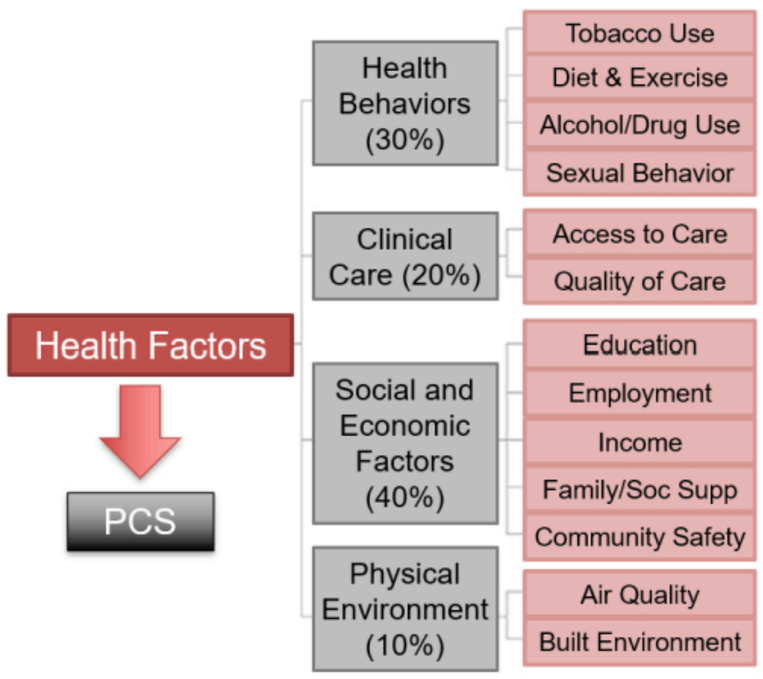
N/A

BEFORE FINAL SUBMISSION, please review the PI checklist to ensure that you have completed all necessary steps. This will increase the likelihood of submitting a feasible and successful proposal.

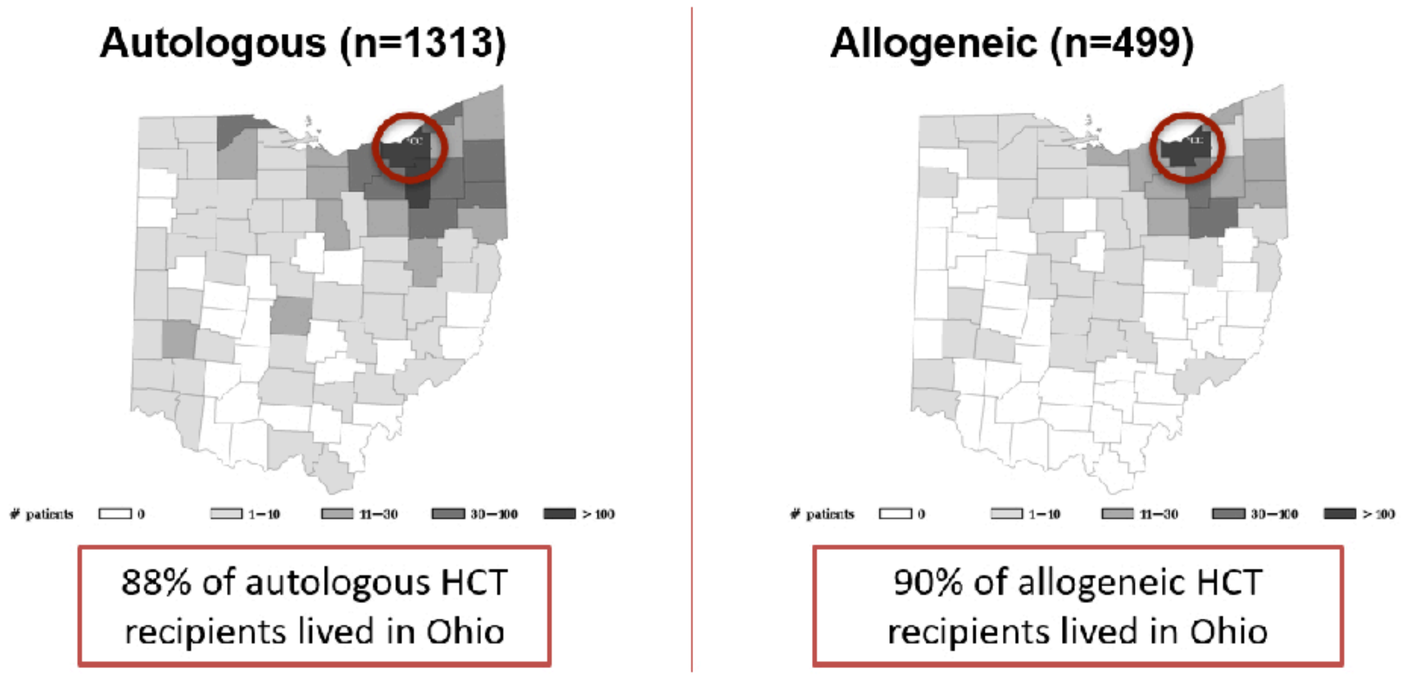
Embedded Data:

N/A

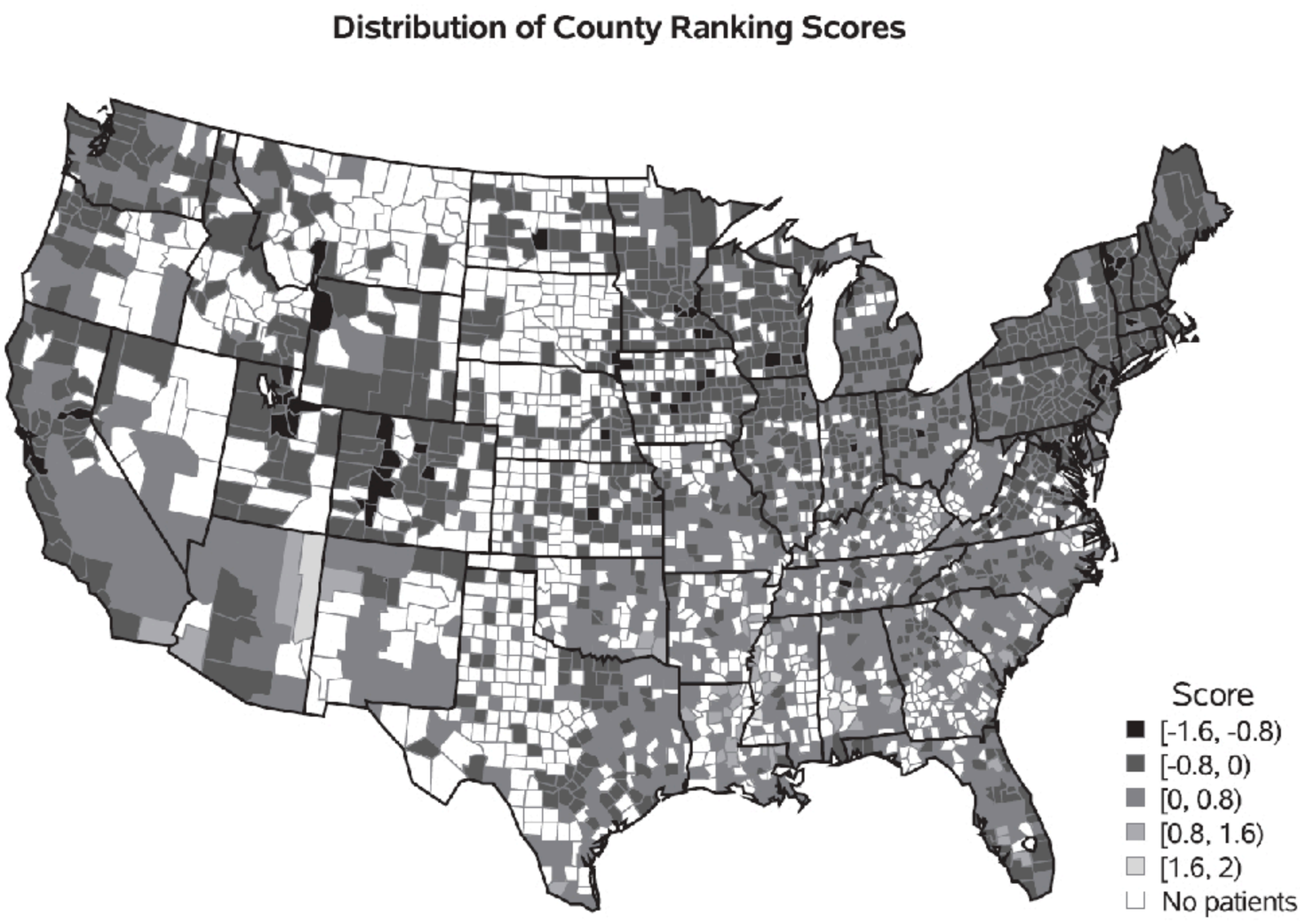
Figure 1A



B



C



A. CHRR health factors measured across four different categories: health behaviors, clinical care, social and economic factors, and physical environment, are weighted to generate the Patient Community Score (PCS).[2]
B. The majority of patients in our recent study lived in Ohio and furthermore, mainly lived near the transplant center, encircled in red. This highlights the limited geographic distribution of this single-center study.[13]
C. Map of county ranking scores based on 2018 CHRR data on adult allogeneic HCT patient residence in the United States. Better health factor rankings are represented by darker colors. White areas did not have transplant recipients.[1]

Characteristics of patients who received first allogeneic and autologous transplant, survived for at least 1 year after transplant and whose primary disease relapsed or progressed was not <1 year post-HCT from 2015 to 2017 reported to the CIBMTR

Characteristic	Allo-HCT	Auto-HCT
No. of patients	3688	2990
No. of centers	148	120
Recipient's age in years - no. (%)		
Median (min-max)	56 (18-80)	59 (18-78)
18-28	458 (12)	89 (3)
29-38	332 (9)	141 (5)
39-48	476 (13)	325 (11)
49-58	828 (22)	852 (28)
59 and above	1594 (43)	1583 (53)
Sex - no. (%)		
Male	2172 (59)	1625 (54)
Female	1516 (41)	1365 (46)
Race - no. (%)		
White	2877 (78)	1757 (59)
Black or African American	424 (11)	981 (33)
Asian	224 (6)	142 (5)
Native Hawaiian or other Pacific Islander	15 (0)	4 (0)
American Indian or Alaska Native	18 (0)	31 (1)
Missing	130 (4)	75 (3)
Disease indication for Transplant - no. (%)		
AML	1218 (33)	6 (0)
ALL	425 (12)	2 (0)
CLL	88 (2)	0 (0)
CML	70 (2)	0 (0)
MDS	905 (25)	0 (0)
Other acute leukemia	44 (1)	0 (0)
NHL	285 (8)	603 (20)
HD	95 (3)	208 (7)
PCD	61 (2)	2152 (72)
ST	3 (0)	13 (0)
SAA	202 (5)	0 (0)
Inherited abnormalities of erythrocyte differentiation	67 (2)	1 (0)
Disorders of the immune system	19 (1)	2 (0)
Inherited disorders of metabolism	2 (0)	0 (0)

Characteristic	Allo-HCT	Auto-HCT
Histiocytic disorders	8 (0)	1 (0)
Autoimmune disease	1 (0)	2 (0)
Other disease	2 (0)	0 (0)
Myeloproliferative Neoplasms	193 (5)	0 (0)
Graft Source - no. (%)		
Bone Marrow	722 (20)	2 (0)
Peripheral blood	2615 (71)	2988 (100)
Cord blood	351 (10)	0 (0)
GVHD prophylaxis - no. (%)		NA
No GVHD prophylaxis	17 (0)	
Ex-vivo T-cell depletion	22 (1)	
CD34 selection	123 (3)	
Post-CY + other(s)	737 (20)	
Post-CY alone	40 (1)	
TAC + MMF +- other(s) (except post-CY)	499 (14)	
TAC + MTX +- other(s) (except MMF, post-CY)	1428 (39)	
TAC + other(s) (except MMF, MTX, post-CY)	205 (6)	
TAC alone	76 (2)	
CSA + MMF +- other(s) (except post-CY)	247 (7)	
CSA + MTX +- other(s) (except MMF, post-CY)	122 (3)	
CSA + other(s) (except MMF, MTX, post-CY)	9 (0)	
CSA alone	19 (1)	
Other(s)	44 (1)	
Missing	100 (3)	
Marital status - no. (%)		
Single, never married	644 (17)	427 (14)
Married	2455 (67)	1898 (63)
Separated	49 (1)	37 (1)
Divorced	240 (7)	308 (10)
Widowed	82 (2)	96 (3)
Missing	218 (6)	224 (7)
Donor type - no. (%)		NA
HLA-identical sibling	860 (23)	
Other related	716 (19)	
Well-matched unrelated (8/8)	1525 (41)	
Partially-matched unrelated (7/8)	210 (6)	
Mis-matched unrelated (<= 6/8)	15 (0)	
Multi-donor	4 (0)	

Characteristic	Allo-HCT	Auto-HCT
Unrelated (matching TBD)	6 (0)	
Cord blood	351 (10)	
Missing	1 (0)	
Time from diagnosis to transplant, months- no. (%)		
<3	220 (6)	77 (3)
3-5	1185 (32)	735 (25)
6-8	595 (16)	883 (30)
9-11	272 (7)	352 (12)
>12	1416 (38)	943 (32)
Zip code available - no. (%)		
Yes	3688 (100)	2990 (100)
Year of transplant - no. (%)		
2015	1247 (34)	949 (32)
2016	1237 (34)	1056 (35)
2017	1204 (33)	985 (33)
Retrieval - no. (%)		
CRF	3688 (100)	2990 (100)
Follow-up, months - median (range)	48 (12-79)	48 (12-83)

Response Summary:

This form is intended to be completed by a physician/researcher for the purpose of proposing a study. Content should not include Personal Identifiable Information (PII) or Protected Health Information (PHI). If you are a patient, do not complete this form. Patients: Contact your healthcare provider immediately for reports of problems with your treatment or problems with products received for your treatment. The CIBMTR uses de-identified data and is unable to associate reported treatment problems, adverse events, or corrections of information with a center, clinical trial, or healthcare provider.

Q1. Study Title

Outcomes of Hispanic Adolescents and Young Adults (AYA) with Acute Lymphoblastic Leukemia After Allogeneic Stem Cell Transplant.

Q2. Key Words

acute lymphoblastic leukemia, allogeneic stem cell transplant, hispanics

Q3. PRINCIPAL INVESTIGATOR

Provide the following information for each investigator:

Principal Investigator #1:

First and last name, degree(s):	Arjun Datt Law, MBBS, MD, DM
Email address:	Arjun.Law@uhn.ca
Institution name:	Hans Messner Allogeneic Blood and Marrow Transplant Program, Princess Margaret Cancer Centre, Toronto
Academic rank:	Assistant Professor

Q4. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- Yes

Q5. Do you identify as an underrepresented/minority?

- Yes

Q6. Principal Investigator #2 (If applicable):

First and last name, degree(s):	Tommy Alfaro Moya
Email address:	tommy.alfaromoya@uhn.ca
Institution name:	Hans Messner Allogeneic Blood and Marrow Transplant Program, Princess Margaret Cancer Centre, Toronto
Academic rank:	Clinical Fellow

Q7. Junior investigator status (defined as <40 years of age and/or ≤5 years from fellowship)

- Yes

Q8. Do you identify as an underrepresented/minority?

- Yes

Q9. We encourage a maximum of two Principal Investigators per study. If more than one author is listed, please indicate who will be identified as the corresponding PI below:

N/A

Q10. If you are a junior investigator and would like assistance identifying a senior mentor for your project please click below:

- Yes, I am a junior investigator and would like assistance identifying a senior mentor for my project

LETTER OF COMMITMENT:

Please note: *A letter of commitment will be signed by Lead and Last authors as it describes the expectations for filling that role. By signing the letter of commitment, the authors accept their responsibilities and will be held accountable for timely completion of all steps in the project. More details regarding author responsibilities can be found here:* *https://www.cibmtr.org/Studies/Observational/StudyManagement/p*

Q12. CURRENT ONGOING WORK WITH CIBMTR: Please list any ongoing CIBMTR projects that you are currently involved in and briefly describe your role.

N/A

Q13. PROPOSED WORKING COMMITTEE:

- Health Services and International Studies

Q14. Please indicate if you have already spoken with a scientific director or working committee chair regarding this study.

- No

Q15. RESEARCH QUESTION:

What are the determinants of outcomes for Hispanic patients diagnosed with Acute Lymphoblastic Leukemia after Allogeneic Stem Cell Transplant.

Q16. RESEARCH HYPOTHESIS:

Hispanic patients with ALL are likely to have reduced access to transplant due to financial and social barriers. They are also more likely to have high-risk disease (Ph-like ALL) or delayed referral to transplant (CR2 instead of CR1) which further impacts outcomes. Representation in clinical trials and access to cellular therapy for ALL is also likely to be limited.

Q17. SPECIFIC OBJECTIVES/OUTCOMES TO BE INVESTIGATED (Include Primary, Secondary, etc.)

Suggested word limit of 200 words:

1. To assess OS, RFS, and GRFS in Hispanic patients diagnosed with ALL undergoing allogeneic stem cell transplantation (AlloHCT)
2. To identify social and societal determinants of health contributing to adverse outcomes in ALL patients undergoing AlloHCT

Q18. SCIENTIFIC IMPACT: Briefly state how the completion of the aims will impact participant care/outcomes and how it will advance science or clinical care.

1. This study will assist in framing recommendations regarding AlloHCT in Hispanic patients with ALL.
2. We aim to identify social and societal determinants of health that are potentially modifiable to improve the outcomes of this population.
3. Determine modifiable factors that prevent higher enrollment in clinical trials.
4. Determine the outcomes of AlloHCT in these patients and examine the factors affecting disease relapse and overall survival.

Q19. SCIENTIFIC JUSTIFICATION: Provide a background summary of previous related research and their strengths and weaknesses, justification of your research and why your research is still necessary.

According to the US Department of Health and Human Services Office of Minority Health Hispanics are the second largest racial ethnic group after non-Hispanic whites. With 62.1 million people they represent the 18.9% of the total US population. There is strong evidence that the incidence of acute lymphoblastic leukemia (ALL) is higher in Hispanics.(1) Hispanics have a higher incidence of a gene
expression profile similar to Philadelphia Chromosome without the t(9;22) and usually carry inherited variants of the GATA3.(2) The Ph chromosome like expression profile is seen in up to 35% of all the cases of ALL in Hispanics. Ph chromosome like ALL usually carry deletions in the IKAROS family zinc finger 1 (IKZF1), the incidence is as high as 80%, up to 50% of these patients present overexpression of cytokine receptor-like factor 2 (CRLF2) and up to half of those patients also have concomitant mutations of JAK-STAT(3). These mutations are the ones most found however, there are mutations in JAK2, ABL1, ABL2 that are also common.(1,4)
Hispanics represent up to 68% of all the cases of Philadelphia Chromosome like ALL. Unfortunately, they also present lower incidence of good prognosis mutations like RUNX1. (1)
When treated with standard chemotherapy regimens Ph like ALL is associated with inferior responses and particularly with persistence of minimal residual disease (MRD). (2)
One recent study by Aldoss et al described a similar outcome after Allo-SCT for Ph Like and other B cell ALL with 3 year post Allo-SCT OS of 43% vs 50%.(5) The use of myeloablative conditioning regimens seems to bypass the negative prognosis of MRD positivity.
Several studies have examined biological differences between ethnic groups and their outcomes regarding response to treatment. Baker et al found that ethnic minorities are more likely to receive Allo-SCT more than a year after diagnosis compared with whites.(6) Hispanics struggle with lower socioeconomic status, language barrier, reduced medication adherence, higher rates of obesity, altered drug metabolism and lower rates of clinical trial enrolment and underrepresentation in National Bone Marrow Donor Program (NMDP).(7–9) It was demonstrated on a recent publication by Schraw et al that Hispanic children with ALL have a poorer OS and EFS when compared to non-Hispanic whites.(7) Mortality for Hispanic children is 1.5 times higher than non-Hispanic whites. Social and societal determinants of health contribute negatively to the already adverse genetic profile of these patients.(10) Hispanics are less likely to interact with the healthcare systems, and they trend to trust less the institutions providing care.(8)

Q19a. SCIENTIFIC JUSTIFICATION: If applicable, upload graphic as a single file (JPG, PNG, GIF)

N/A

Q20. PARTICIPANT SELECTION CRITERIA: State inclusion and exclusion criteria.

1. All patients of Hispanic descent >17 years old with ALL, with variants determined by conventional karyotyping, PCR analysis or NGS sequencing, who have received Allo-SCT, will be included in the analyses

Q21. Does this study include pediatric patients?

- No

Q21a. If this study does not include pediatric patients, please provide justification:

Outcomes of pediatric Acute lymphoblastic leukemia are significantly superior to the ones of AYA and adults, most pediatric patients do not undergo allogeneic stem cell transplantation for ALL.

Q22. DATA REQUIREMENTS: After reviewing data on CIBMTR forms, list patient-, disease- and infusion-variables to be considered in the multivariate analyses. Data collection forms available at: http://www.cibmtr.org/DataManagement/DataCollectior Outline any supplementary data required. Additional data collection is extremely difficult and will make your proposal less feasible.

Data on the following will be retrieved: age, sex, diagnosis (ALL and its variants), date of diagnosis, cytogenetics, molecular studies, prior treatment received before transplant, number of prior HSCT (auto and/or allo HSCT), disease status at time of transplant, KPS at time of transplant, date of transplant, number of lines of chemotherapy prior to transplant, date of transplant, donor (related, unrelated, haploidentical, cord), HLA match, donor sex, donor and recipient CMV status, product type of stem cells (bone marrow, peripheral blood, single cord, double cord), conditioning regimen, GVHD prophylaxis, time to neutrophil and platelet engraftment, aGVHD grade and cGVHD grade, date of diagnosis of aGVHD and cGVHD, date of relapse, and date and cause of death.

Q23. **PATIENT REPORTED OUTCOME (PRO) REQUIREMENTS: If the study requires PRO data collected by CIBMTR, the proposal should include: 1) A detailed description of the PRO domains, timepoints, and proposed analysis of PROs; 2) A description of the hypothesis specific to PROS.**

For additional information on what PRO measures have been collected and timepoints of collection, please reach out to the Late Effects and Quality of Life or Health Services Working Committee leadership: https://www.cibmtr.org/About/WhoWeAre/Com

N/A

Q24. **SAMPLE REQUIREMENTS: If the study requires biologic samples from the CIBMTR Repository, the proposal should also include: 1) A detailed description of the proposed testing methodology and sample requirements; 2) A summary of the investigator's previous experience with the proposed assay systems. PIs should be encouraged to review the inventory details, sample types collected and reach out to research_repos@nmdp.org with any questions.**

More information can be found at: https://www.cibmtr.org/Samples/Inventory/Pages/index

None required

Q25. NON-CIBMTR DATA SOURCE: If applicable, please provide: 1) A description of external data source to which the CIBMTR data will be linked; 2) The rationale for why the linkage is required, i.e., neither database contains all the data required to answer the study question.

None required

Q26. REFERENCES:

1. Quiroz E, Aldoss I, Pullarkat V, Rego E, Marcucci G, Douer D. The emerging story of acute lymphoblastic leukemia among the Latin American population – biological and clinical implications. Blood Rev. 2019 Jan;33:98–105.
2. Pui CH, Roberts KG, Yang JJ, Mullighan CG. Philadelphia Chromosome–like Acute Lymphoblastic Leukemia. Clin Lymphoma Myeloma Leuk. 2017 Aug;17(8):464–70.
3. Muffly L, Yin J, Jacobson S, Wall A, Quiroz E, Advani AS, et al. Disparities in trial enrollment and outcomes of Hispanic adolescent and young adult acute lymphoblastic leukemia. Blood Adv. 2022 Jul 26;6(14):4085–92.
4. Jain N, Roberts KG, Jabbour E, Patel K, Eterovic AK, Chen K, et al. Ph-like acute lymphoblastic leukemia: a high-risk subtype in adults. Blood. 2017 Feb 2;129(5):572–81.
5. Aldoss I, Yang D, Tomasian V, Mokhtari S, Jackson R, Gu Z, et al. Outcomes of allogeneic hematopoietic cell transplantation in adults with fusions associated with Ph-like ALL. Blood Adv. 2022 Sep 13;6(17):4936–48.
6. Baker KS, Loberiza FR, Yu H, Cairo MS, Bolwell BJ, Bujan-Boza WA, et al. Outcome of Ethnic Minorities With Acute or Chronic Leukemia Treated With Hematopoietic Stem-Cell Transplantation in the United States. J Clin Oncol. 2005 Oct 1;23(28):7032–42.
7. Kahn JM, Keegan THM, Tao L, Abrahão R, Bleyer A, Viny AD. Racial disparities in the survival of American children, adolescents, and young adults with acute lymphoblastic leukemia, acute myelogenous leukemia, and Hodgkin lymphoma: Survival Outcomes in Leukemia and Lymphoma. Cancer. 2016 Sep 1;122(17):2723–30.
8. Khullar D, Chokshi DA. Challenges for immigrant health in the USA—the road to crisis. The Lancet. 2019 May;393(10186):2168–74.
9. Gragert L, Eapen M, Williams E, Freeman J, Spellman S, Baitty R, et al. HLA Match Likelihoods for Hematopoietic Stem-Cell Grafts in the U.S. Registry. N Engl J Med. 2014 Jul 24;371(4):339–48.
10. Schraw JM, Peckham-Gregory EC, Hughes AE, Scheurer ME, Pruitt SL, Lupo PJ. Residence in a Hispanic Enclave Is Associated with Inferior Overall Survival among Children with Acute Lymphoblastic Leukemia. Int J Environ Res Public Health. 2021 Sep 2;18(17):9273.

Q27. **CONFLICTS OF INTEREST: Do you have any conflicts of interest pertinent to this proposal concerning:**

1. Employment (such as an independent contractor, consultant or providing expert testimony)?
2. Relationships (such as executive and advisory committee positions, medical consultant, speaker's bureau)?
3. Ownership (such as equity, ownership or financial interests)?
4. Transactions (such as honoraria, patents, royalties and licenses)?
5. Legal (such as pending or current arbitration or legal proceedings)?

- No, I do not have any conflicts of interest pertinent to this proposal

Q27a. **If yes, provide detail on the nature of employment, name of organization, role, entity, ownership, type of financial transaction or legal proceeding and whether renumeration is >$5000 annually.**

N/A

BEFORE FINAL SUBMISSION, please review the PI checklist to ensure that you have completed all necessary steps. This will increase the likelihood of submitting a feasible and successful proposal.

Embedded Data:

N/A

Table 1: Characteristics of hispanic patients who received first allogeneic transplant for ALL above the age of 17 years from 2008 to 2019 registered with CIBMTR.

Characteristic	TED	CRF	Total
No. of patients	1689	659	2348
No. of centers	179	113	186
Recipient's age in years - no. (%)			
Median (min-max)	34 (17-72)	33 (17-71)	34 (17-72)
18-28	651 (39)	261 (40)	912 (39)
29-38	339 (20)	139 (21)	478 (20)
39-48	343 (20)	114 (17)	457 (19)
49-58	240 (14)	92 (14)	332 (14)
59 and above	116 (7)	53 (8)	169 (7)
Sex - no. (%)			
Male	997 (59)	379 (58)	1376 (59)
Female	692 (41)	280 (42)	972 (41)
Race - no. (%)			
White	1230 (73)	510 (77)	1740 (74)
Black or African American	18 (1)	18 (3)	36 (2)
Asian	2 (0)	7 (1)	9 (0)
Native Hawaiian or other Pacific Islander	8 (0)	4 (1)	12 (1)
American Indian or Alaska Native	24 (1)	8 (1)	32 (1)
Missing	407 (24)	112 (17)	519 (22)
Ethnicity - no. (%)			
Hispanic or Latino	1689 (100)	659 (100)	2348 (100)
Disease indication for Transplant - no. (%)			
ALL	1689 (100)	659 (100)	2348 (100)
Graft Source - no. (%)			
Bone Marrow	273 (16)	109 (17)	382 (16)
Peripheral blood	1341 (79)	371 (56)	1712 (73)
Cord blood	75 (4)	179 (27)	254 (11)
GVHD prophylaxis - no. (%)			
No GVHD prophylaxis	0 (0)	2 (0)	2 (0)

Characteristic	TED	CRF	Total
Ex-vivo T-cell depletion	18 (1)	4 (1)	22 (1)
CD34 selection	33 (2)	22 (3)	55 (2)
Post-CY + other(s)	236 (14)	135 (20)	371 (16)
Post-CY alone	14 (1)	3 (0)	17 (1)
TAC + MMF +- other(s) (except post-CY)	96 (6)	91 (14)	187 (8)
TAC + MTX +- other(s) (except MMF, post-CY)	679 (40)	206 (31)	885 (38)
TAC + other(s) (except MMF, MTX, post-CY)	176 (10)	40 (6)	216 (9)
TAC alone	52 (3)	14 (2)	66 (3)
CSA + MMF +- other(s) (except post-CY)	133 (8)	94 (14)	227 (10)
CSA + MTX +- other(s) (except MMF, post-CY)	177 (10)	34 (5)	211 (9)
CSA + other(s) (except MMF, MTX, post-CY)	4 (0)	6 (1)	10 (0)
CSA alone	29 (2)	4 (1)	33 (1)
Other(s)	17 (1)	4 (1)	21 (1)
Missing	25 (1)	0 (0)	25 (1)
Conditioning regimen - no. (%)			
MAC	1396 (83)	257 (39)	1653 (70)
RIC/NST	276 (16)	35 (5)	311 (13)
Missing	17 (1)	367 (56)	384 (16)
Year of transplant - no. (%)			
2008	74 (4)	70 (11)	144 (6)
2009	101 (6)	48 (7)	149 (6)
2010	119 (7)	35 (5)	154 (7)
2011	111 (7)	37 (6)	148 (6)
2012	129 (8)	38 (6)	167 (7)
2013	138 (8)	56 (8)	194 (8)
2014	133 (8)	67 (10)	200 (9)
2015	142 (8)	55 (8)	197 (8)
2016	153 (9)	60 (9)	213 (9)
2017	183 (11)	52 (8)	235 (10)
2018	187 (11)	67 (10)	254 (11)
2019	219 (13)	74 (11)	293 (12)

end of table

I. Study Title:

Characterizing differences in the clinical outcomes of commercial CAR T-cells for B-cell lymphoma, ALL, and multiple myeloma based on race/ ethnicity, sex, and socioeconomic status

II. Key Words: Cellular Therapies, Chimeric Antigen Receptor Therapy, CAR-T, Cytokine Release Syndrome, CRS, Distress Community Index, DCI, Diffuse Large B-cell Lymphoma, Diversity, Disparities, Follicular Lymphoma, ICANS, Immune Effector Cell-Associated Neurotoxicity Syndrome, Leukemia, Lymphoma, Mantle Cell Lymphoma, Multiple Myeloma, Neurotoxicity, Race, Racial Disparities, Sex, Socioeconomic Status, Treatment Toxicity, community health

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Current Ongoing Work with CIBMTR: None

IV. Proposed Working Committee

Health Services and International Studies

V. Research Questions:

Are sociodemographic factors (race/ethnicity, sex, socioeconomic status, geographic location) associated with the clinical outcomes of commercial CAR T-cells for patients with relapsed/refractory (R/R) B-cell lymphoma (large B-cell lymphoma [LBCL], mantle cell lymphoma [MCL], follicular lymphoma [FL)], B-ALL, and myeloma?

VI. Research Hypotheses

1. We hypothesize that sex, racial/ ethnic, socioeconomic status, and geographic differences influence the clinical outcomes & toxicities following commercial CAR-T therapy for patients with R/R B-cell lymphoma, B-ALL, and Myeloma

VII. Specific Objectives/Outcomes to be Investigated

Primary Objective:

1. Outcomes: Evaluate differences in outcomes following commercial CAR-T for patients with R/R B-cell lymphoma, ALL, and myeloma, by sex, race/ethnicity, socioeconomic status (community health score derived from zip code[1]), and geographic location.
   a. Treatment response: CR rate and PFS at 6 months
   b. Toxicity: grades 3-5 CRS & ICANS as per CIBMTR adjudicated ASTCT grading[2]

Secondary objective:

2. Develop a prediction model for CAR-T short-term (≤ 6 months) outcomes in adults with relapsed/refractory B-Cell malignancies (NHL, ALL, PCD).

Primary Outcomes:

1. Toxicity: grades 3-5 cytokine release syndrome (CRS) or neurotoxicity (ICANS) at Day 0/1, Day 100, 6 months, 1 year, and 2 years.
2. Treatment response: Complete Remission (CR) rate and progression free survival (PFS) at 6 months, 1 year, and 2 years.

VIII. Scientific Impact

This research will improve our understanding of disparities in the outcomes of cellular therapies. The prediction model results will inform novel personalized risk-adapted clinical management strategies for patients receiving CAR-T. Evaluation of individual- and community-level factors could extend opportunities for cellular therapy to improve predictions of individual risk of toxicity, immune system dysfunction and non-relapsed mortality. Study results will inform existing risk strategies for predicting toxicity, early interventions post-CAR-T infusions, and identification of barriers to access that would influence treatment toxicity outcomes.

The ultimate aim is to be able to identify specific patient groups at special risk for compromised care. This information is a pre-requisite to further efforts at the institutional and national levels to enhance cell therapy outcomes and care delivery, and will underpin critically important efforts to diversify patient populations, mitigate barriers to care, and maximize the equitable provision of cellular therapies for less or under-privileged groups. Furthermore, the issue of equitable outcomes of CAR T-cell therapies is becoming increasingly important, as these therapies are rapidly expanding in the U.S.

IX. Scientific Justification:

CAR-T therapy has transformed the landscape of treatment paradigms for several hematologic malignancies including B-cell lymphomas, B-ALL, and multiple myeloma. For example, in the

JULIET and ZUMA-1 phase II trials and TRANSCEND NHL 001 phase I trial, patients with relapsed/refractory LBCL who received CD-19 directed CAR-T therapy showed significant improvement in progression free survival and overall survival, with long-term survival in 30-40% in a patient population which had already received autoHCT or two lines of therapy.[3-6] These encouraging results led to the approval by the US FDA of three CAR T cell products for commercial use in this population, axicabtagene ciloleucel, tisagenlecleucel. and lisocabtagene maraleucel. Axicabtagene ciloleucel, tisagenlecleucel were both approved as second line therapy for LBCL based on the ZUMA-7 and TRANSFORM trials meeting their primary endpoints in favor of CAR T over standard of care.[7-8] In 2018, Tisagenlecleucel was also FDA approved for treatment of pediatric and young adult patients with R/R B-ALL.[9] Additionally, two B-cell maturation antigen (BCMA) targeting CAR T cells products have been approved by the FDA for treatment of multiple myeloma, idecabtagene vicleucel (ide-cel, Abecma®) and ciltacabtagene autoleucel (cilta-cel; Carvykti®).[10] Several "real world" retrospective studies of patients treated with commercial axicabtagene ciloleucel or tisagenlecleucel showed rates of responses and toxicities similar to these pivotal clinical trials.[11-12]

However, recent work by Ahmed et al.[13] described racial and socioeconomic disparities in the access to CAR-T for LBCL, B-ALL, and Myeloma. The authors queried the Vizient clinical database and found that African Americans were less likely than other racial/ethnic groups to receive CAR T cell therapy, and that, of CAR-T related admissions, only 7.3% were from patients from neighborhoods with a mean income <$40,000 and few CAR-T patients had Medicaid or were uninsured. Both this analysis and that by Snyder et al.[14] found that CAR-T patients who were from communities further away from the transplant center were from higher socioeconomic status (SES) groups.

Recently, Faruqi et al.[15] analyzed data from 5 phase 1 NCI clinical trials in CAR-T for B-ALL including 139 patients, and found that Hispanic patients had 4.5 times the odds of severe cytokine release syndrome (compared to White/ non-Hispanic patients). However, no analysis has examined racial/ ethnic or SES disparities in treatment outcomes or toxicities in B-cell lymphomas or myeloma. Furthermore, given the analysis by Faruqi et al. was in the clinical trials setting, the results may not apply to standard practice as insurance status and toxicity monitoring protocols may differ. With this proposal, we seek to answer these questions, and also to validate the findings of Faruqi et al. through the CIBMTR database.

Sociodemographic factors have previously been shown to be associated with outcomes of diseases for which commercial CAR-T therapies are indicated, as well as for allogeneic transplantation other similarly complex procedures such as hematopoietic cell transplantation.[16-22] Additionally, a recent survey-based analysis of patient with LBCL demonstrated that, for Black patients, requirement to travel was an important independent negative factor in choosing a hypothetical treatment which was only offered at a distant cancer center.[23] Based on these results, we hypothesize that sociodemographic factors are likely to be associated with CAR-T therapy outcomes as well.

Example of Variation in Community Health Indicators for PIs' Cancer Centers (Justification for use of multiple measures of community health and distress).

	Rutgers CINJ 08903	MSKCC 10065	Duke Cancer Center 27710	OSUCCC 43210

Community Distress Index	90.4 (Distressed)	7.3 (Prosperous)	79.2 (At-Risk)	90.1 (Distressed)
Area Deprivation Index (national)	60th percentile	1st percentile	30th percentile	60th percentile
Social Vulnerability Index	.5961 (medium to high vulnerability)	.2035 (low vulnerability)	.8179 (high vulnerability)	.2401 (low vulnerability)

Furthermore, many lines of evidence describe sex differences in immune responses.[24-25] Additionally, there is ample evidence to suggest immunological and pharmacokinetic differences based on sex. Dosing both men and women with the same exact dose of an immunological therapy without consideration of these differences may impact outcomes and therefore warrants investigation. Compared to males, females mount a more vigorous antibody- and cell-mediated immune responses following either infection or vaccination. Estradiol is associated with upregulation of CD4 T cells and dendritic cells, increased survival of autoreactive B cells, and decreased tumor necrosis factor production.[26-28] Another possible mechanism may lie in the immunosuppressive properties of androgens: a recent study showed that androgen-deprivation therapy allows male mice to mount a more robust immune response, and in humans, genes associated with poor virus-response are up-regulated by androgens.[29] Also men presenting with high serum androgen levels display the weakest influenza immune responses.[30] The sex-specific differences in elderly patients with LBCL appear to have increased with the introduction of the monoclonal CD20 antibody rituximab into the therapeutic armamentarium as seen in the RICOVER- 60 study.[31-32] Several clinical trials since then have tried to optimize the rituximab dosing and timing to improve on the outcomes of patients.[33-35] Solid tumor studies with immune checkpoint inhibitors also suggest differences in the response and toxicities based on sex. Data remains scarce in hematologic malignancies, especially with cellular therapy.

This study also includes the secondary aim to develop a prediction model for CAR-T short-term (≤6 months) outcomes in adults with relapsed/refractory B-Cell malignancies (NHL, ALL, PCD). Krieger et al. (2018) suggests tumor-related factors, poor health outcomes, and overall survival are attributable to race and an individual's exposure to societal dynamics.[36] Accordingly, our model will include any sociodemographic variables which our univariate analyses identify as significantly impacting outcomes and/or toxicity post-cellular therapy. This work will advance efforts to support vulnerable patients undergoing CAR-T, including through informing interventions to address identified disparities.

X. PARTICIPANT SELECTION CRITERIA:

Inclusion criteria:
Adults age 18 and older at time of CAR-T infusion
CAR-T therapy received between January 1, 2016 and December 31, 2022
Disease indication(s): Relapsed/Refractory:
- Large B Cell Lymphoma (LBCL)
- Follicular Lymphoma (FL)
- Mantle Cell Lymphoma (MCL)
- Multiple myeloma (MM)
- Acute lymphoblastic leukemia (ALL)

CAR-T agents:
- Axicabtagene ciloleucel
- Tisagenlecleucel

- Lisocabtagene maraleucel
- Idecabtagene vecleucel
- Brexucatagene autoleucel
- Ciltacabtagene autoleucel

Exclusion criteria:
- Treated at a cancer center outside of the United States
- Patients treated on clinical trial

XI. Data Requirements:

Data Elements:

Patient-related: Age at cell infusion, Date of infusion, BMI, Functional status score at CAR-T infusion (ECOG or Karnofsky), Comorbidities, Infectious disease status pre-infusion, Time to toxicity, smoking/alcohol/recreational drug exposure

Disease-related: Disease indication, Disease burden by flow cytometry, Types of disease, disease stage, prognostic score and type when applicable, Number of prior therapies before cell therapy

Cell therapy-related: Time from diagnosis to cell therapy, Time from leukopheresis to infusion, Lymphodepleting regimen, Toxicity Prophylactic or treatment (i.e., tocilizumab, other IL 6 blocker), Prior autologous and/or allogeneic transplantation.

CAR-T Related: Cell dose, Infused cellular therapy product(s)

Patient Sociodemographic: Race, Ethnicity, sex, zip code of patient residence

Cancer Center Related: FACT accreditation, NCI designation, Volume (CAR T, HCT, both) (2016 - 2021), region, zip code

Outcomes: Cytokine Release Syndrome: any and grade 3-4, time to onset; Neurotoxicity (ICANS): any and grade 3-4, time to onset; Other toxicities; Hospitalized post-infusion; CR rate=complete response rate; OR=overall response; ORR=overall response rate; PFS=progression-free survival; Death, Cause of death, date patient last known to be alive

PATIENT REPORTED OUTCOME (PRO) REQUIREMENTS: none

SAMPLE REQUIREMENTS: none

NON-CIBMTR DATA SOURCE:

Community Health Measures linked on patient and cancer center zip code:
- Community Distress Index (https://eig.org/distressed-communities/)
- Area Deprivation Index (https://www.neighborhoodatlas.medicine.wisc.edu/)
- Social Vulnerability Index (https://www.atsdr.cdc.gov/placeandhealth/svi/index.html)

- County Health Rankings (https://www.countyhealthrankings.org/), based on
- Rural-Urban Commuting Area (RUCA) (https://www.ers.usda.gov/data-products/rural-urban-commuting-area-codes.aspx)
- Rural-Urban Continuum Codes (RUCC) (https://www.ers.usda.gov/data-products/rural-urban-continuum-codes.aspx)

Cancer Center Variables:
- FACT accreditation
- NCI designation
- Volume (CAR T, HCT, both) (2016 - 2021)

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CONFLICTS OF INTEREST: None

Table 1: Characteristics of patients who received cell therapy after 2016 per event, aged 18 and above years in USA registered with CIBMTR.

Characteristic	ALL	Follicular NHL	DLBCL	MCL	PCD/MM	Total
No. of infusions	399	338	4779	478	678	6672
No. of centers	101	81	120	80	62	146
CT infusion counting number - no. (%)						
1	352 (88)	337 (100)	4727 (99)	474 (99)	658 (97)	6548 (98)
2	43 (11)	1 (0)	47 (1)	4 (1)	19 (3)	114 (2)
3	4 (1)	0 (0)	5 (0)	0 (0)	1 (0)	10 (0)
Age at infusion, by category - no. (%)						
Median (min-max)	23 (18-79)	62 (29-87)	64 (18-91)	67 (34-85)	65 (23-86)	63 (18-91)
18- 19 years	100 (25)	0 (0)	9 (0)	0 (0)	0 (0)	109 (2)
20- 29 years	225 (56)	1 (0)	125 (3)	0 (0)	2 (0)	353 (5)
30- 39 years	27 (7)	6 (2)	254 (5)	4 (1)	7 (1)	298 (4)
40- 49 years	10 (3)	37 (11)	426 (9)	16 (3)	38 (6)	527 (8)
50- 59 years	18 (5)	92 (27)	1039 (22)	78 (16)	165 (24)	1392 (21)
60- 69 years	18 (5)	130 (38)	1642 (34)	210 (44)	291 (43)	2291 (34)
70+ years	1 (0)	72 (21)	1284 (27)	170 (36)	175 (26)	1702 (26)
Recipient Gender - no. (%)						
Male	240 (60)	207 (61)	3010 (63)	366 (77)	403 (59)	4226 (63)

Characteristic	ALL	Follicular NHL	DLBCL	MCL	PCD/MM	Total
Female	159 (40)	130 (38)	1768 (37)	111 (23)	271 (40)	2439 (37)
Missing	0 (0)	1 (0)	1 (0)	1 (0)	4 (1)	7 (0)
CAR-T - no. (%)						
Commercial Car-T	399 (100)	338 (100)	4779 (100)	478 (100)	678 (100)	6672 (100)
Recipient ethnicity by race - no. (%)						
White						
Hispanic or Latino	134 (34)	25 (7)	348 (7)	33 (7)	37 (5)	577 (9)
Not Hispanic or Latino	155 (39)	253 (75)	3404 (71)	374 (78)	501 (74)	4687 (70)
Non-resident of the U.S.	1 (0)	2 (1)	34 (1)	1 (0)	0 (0)	38 (1)
Unknown	2 (1)	7 (2)	83 (2)	5 (1)	4 (1)	101 (2)
Black or African American						
Hispanic or Latino	1 (0)	1 (0)	8 (0)	0 (0)	0 (0)	10 (0)
Not Hispanic or Latino	30 (8)	18 (5)	262 (5)	21 (4)	92 (14)	423 (6)
Non-resident of the U.S.	0 (0)	0 (0)	1 (0)	0 (0)	0 (0)	1 (0)
Unknown	0 (0)	1 (0)	2 (0)	0 (0)	1 (0)	4 (0)
Asian						
Hispanic or Latino	0 (0)	0 (0)	1 (0)	0 (0)	0 (0)	1 (0)
Not Hispanic or Latino	13 (3)	12 (4)	251 (5)	12 (3)	15 (2)	303 (5)
Non-resident of the U.S.	0 (0)	0 (0)	4 (0)	0 (0)	0 (0)	4 (0)
Unknown	0 (0)	0 (0)	4 (0)	0 (0)	0 (0)	4 (0)
Native Hawaiian or other Pacific Islander						
Not Hispanic or Latino	0 (0)	0 (0)	10 (0)	0 (0)	1 (0)	11 (0)
Unknown	0 (0)	0 (0)	0 (0)	0 (0)	1 (0)	1 (0)
American Indian or Alaska Native						
Hispanic or Latino	1 (0)	0 (0)	5 (0)	0 (0)	0 (0)	6 (0)

Characteristic	ALL	Follicular NHL	DLBCL	MCL	PCD/MM	Total
Not Hispanic or Latino	1 (0)	1 (0)	9 (0)	1 (0)	2 (0)	14 (0)
Non-resident of the U.S.	0 (0)	0 (0)	1 (0)	0 (0)	0 (0)	1 (0)
Unknown	0 (0)	0 (0)	0 (0)	1 (0)	0 (0)	1 (0)
Other						
Hispanic or Latino	2 (1)	0 (0)	2 (0)	0 (0)	0 (0)	4 (0)
Not Hispanic or Latino	6 (2)	0 (0)	25 (1)	2 (0)	3 (0)	36 (1)
Unknown	2 (1)	0 (0)	1 (0)	0 (0)	0 (0)	3 (0)
More than one race						
Hispanic or Latino	27 (7)	7 (2)	101 (2)	8 (2)	6 (1)	149 (2)
Not Hispanic or Latino	2 (1)	5 (1)	67 (1)	4 (1)	4 (1)	82 (1)
Non-resident of the U.S.	0 (0)	0 (0)	4 (0)	0 (0)	0 (0)	4 (0)
Unknown	3 (1)	3 (1)	55 (1)	8 (2)	1 (0)	70 (1)
Missing						
Hispanic or Latino	15 (4)	2 (1)	41 (1)	4 (1)	4 (1)	66 (1)
Not Hispanic or Latino	1 (0)	1 (0)	27 (1)	2 (0)	3 (0)	34 (1)
Non-resident of the U.S.	3 (1)	0 (0)	7 (0)	0 (0)	0 (0)	10 (0)
Unknown	0 (0)	0 (0)	21 (0)	2 (0)	3 (0)	26 (0)
Missing	0 (0)	0 (0)	1 (0)	0 (0)	0 (0)	1 (0)
Age at infusion, by category #2 - no. (%)						
- 39	352 (88)	7 (2)	388 (8)	4 (1)	9 (1)	760 (11)
- 65	39 (10)	193 (57)	2257 (47)	197 (41)	321 (47)	3007 (45)
65+	8 (2)	138 (41)	2134 (45)	277 (58)	348 (51)	2905 (44)
Age at infusion, by category #3 - no. (%)						
- 64	391 (98)	200 (59)	2645 (55)	201 (42)	330 (49)	3767 (56)
65+	8 (2)	138 (41)	2134 (45)	277 (58)	348 (51)	2905 (44)

Characteristic	ALL	Follicular NHL	DLBCL	MCL	PCD/MM	Total
Disease - no. (%)						
Acute lymphoblastic leukemia (ALL)	399 (100)	0 (0)	0 (0)	0 (0)	0 (0)	399 (6)
Non-Hodgkin lymphoma (NHL)	0 (0)	338 (100)	4779 (100)	478 (100)	0 (0)	5595 (84)
Plasma cell disorder/multiple myeloma (PCD/MM)	0 (0)	0 (0)	0 (0)	0 (0)	678 (100)	678 (10)
Clinical trial - no. (%)						
No	394 (99)	332 (98)	4690 (98)	470 (98)	667 (98)	6553 (98)
Yes	5 (1)	6 (2)	89 (2)	8 (2)	11 (2)	119 (2)
Product - no. (%)						
Kymriah	304 (76)	13 (4)	1097 (23)	1 (0)	0 (0)	1415 (21)
Yescarta	0 (0)	313 (93)	3364 (70)	10 (2)	0 (0)	3687 (55)
Tecartus	95 (24)	1 (0)	4 (0)	466 (97)	0 (0)	566 (8)
Breyanzi	0 (0)	11 (3)	314 (7)	1 (0)	0 (0)	326 (5)
Abecma	0 (0)	0 (0)	0 (0)	0 (0)	599 (88)	599 (9)
Carvykti	0 (0)	0 (0)	0 (0)	0 (0)	79 (12)	79 (1)
Types of prior HCTs - no. (%)						
No prior HCT	272 (68)	279 (83)	3632 (76)	324 (68)	91 (13)	4598 (69)
Prior allo-HCT	119 (30)	1 (0)	60 (1)	10 (2)	7 (1)	197 (3)
Prior auto-HCT	1 (0)	57 (17)	1037 (22)	133 (28)	550 (81)	1778 (27)
Prior auto and allo-HCT	1 (0)	0 (0)	11 (0)	6 (1)	20 (3)	38 (1)
Not Reported	6 (2)	1 (0)	39 (1)	5 (1)	10 (1)	61 (1)
Year of CT - no. (%)						
2017	5 (1)	0 (0)	8 (0)	0 (0)	0 (0)	13 (0)
2018	44 (11)	10 (3)	547 (11)	1 (0)	0 (0)	602 (9)
2019	78 (20)	9 (3)	1045 (22)	1 (0)	0 (0)	1133 (17)
2020	73 (18)	14 (4)	1153 (24)	77 (16)	0 (0)	1317 (20)

Characteristic	ALL	Follicular NHL	DLBCL	MCL	PCD/MM	Total
2021	66 (17)	171 (51)	1127 (24)	252 (53)	299 (44)	1915 (29)
2022	133 (33)	134 (40)	899 (19)	147 (31)	379 (56)	1692 (25)
Zip code available - no. (%)						
No	163 (41)	57 (17)	2654 (56)	64 (13)	24 (4)	2962 (44)
Yes	236 (59)	281 (83)	2125 (44)	414 (87)	654 (96)	3710 (56)
Time from receiving H4000 baseline form to infusion, days - median (min-max)	33 (-5-909)	12 (-4-406)	28 (-33-1398)	21 (-5-597)	15 (-11-400)	24 (-33-1398)