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Access to Chimeric Antigen Receptor T Cell Clinical Trials in Underrepresented Populations: A Multicenter Cohort Study of Pediatric and Young Adult Acute Lymphobastic Leukemia Patients

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Chimeric antigen receptor T cell (CAR-T) therapy is a promising approach to improve survival for children and adults with relapsed/refractory (r/r) B cell acute lymphoblastic leukemia (B-ALL), but these clinical trials might not be equally accessible to patients of low socioeconomic status (SES) or to patients from racial or ethnic minority groups. We sought to describe the sociodemographic characteristics of pediatric and adolescent and young adult (AYA) patients enrolled in CAR-T clinical trials and to compare these characteristics to those of other patients with r/r B-ALL. We conducted a multicenter retrospective cohort study at 5 pediatric consortium sites to compare the sociodemographic characteristics of patients treated and enrolled in CAR-T trials at their home institution, other patients with r/r B-ALL treated at these sites, and patients referred from an external hospital for CAR-T trials. The patients were age 0 to 27 years with r/r B-ALL treated at 1 of the consortium sites between 2012 and 2018. Clinical and demographic data were collected from the electronic health record. We calculated distance from home to treating institution and assigned SES scores based on census tract. Among the 337 patients treated for r/r B-ALL, 112 were referred from an external hospital to a consortium site and enrolled in a CAR-T trial and 225 were treated primarily at a consortium site, with 34% enrolled in a CAR-T trial. Patients treated primarily at a consortium site had similar characteristics regardless of trial enrollment. Lower proportions of Hispanic patients (37% versus 56%; $P = .03$), patients whose preferred language was Spanish (8% versus 22%; $P = .006$), and publicly insured patients (38% versus 65%; $P = .001$) were referred from an external hospital than were treated primarily at a consortium site and enrolled in a CAR-T trial. Patients who are Hispanic, Spanish-speaking, or publicly insured are underrepresented in referrals from external hospitals to CAR-T centers. External provider implicit bias also may influence referral of these patients. Establishing partnerships between CAR-T centers and external hospital sites may improve provider familiarity, patient referral, and patient access to CAR-T clinical trials.

INTRODUCTION

B-cell acute lymphoblastic leukemia (B-ALL) is the most common childhood cancer in the United States [1]. Significant advances in the treatment of B-ALL have been made over the last several decades, and more than 85% of children now

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survive without relapse following upfront chemotherapy [1,2]. Although outcomes for B-ALL are generally favorable in children, adolescents, and young adults (AYAs), approximately 15% to 20% of patients experience relapsed or refractory (r/r) disease [1,2]. In patients experiencing first relapse, current 5-year overall survival (OS) is approximately 50% [2]. Chimeric antigen receptor T cell (CAR-T) therapy has revolutionized the treatment of r/r B-ALL over the past decade, with more than 80% of patients achieving a complete remission and approximately 50% achieving durable remission with CAR-T therapy alone [3,4].

Population-based analyses [5,6] and analyses of cooperative group trials [7–9] have consistently demonstrated significantly inferior survival among Black and Hispanic pediatric and AYA patients with B-ALL. These survival disparities persist after adjusting for such important clinical factors as age, WBC count at diagnosis, immunophenotype, and chromosomal abnormalities, suggesting that the disparities may be due to nonbiological factors [7,9]. Low socioeconomic status (SES) also is associated with inferior survival in pediatric and AYA cancer patients. Previous studies have demonstrated that the presence of household-level or neighborhood-level poverty confers significantly inferior survival outcomes [10–15]. Although clinical trials have played a substantial role in improving survival for acute leukemia, disparities in clinical trial enrollment have been well documented among AYAs and minority racial and ethnic groups [1,16,17].

CAR-T clinical trials are restricted to specialized centers owing to the expertise required for collection and administration of the CAR-T product. For many patients and families, participation in a CAR-T clinical trial requires travel with temporary relocation for at least 4 weeks and other disruptions to work and childcare. Previous studies have demonstrated that transportation and distance are significant barriers to healthcare access, particularly for patients of lower SES [18]. Disparities in CAR-T trial enrollment have been previously described in Black patients with multiple myeloma [19].

Although recent investigations of pediatric patients who are able to receive CAR-T therapy have demonstrated similar outcomes regardless of race, ethnicity [20], or SES [21], limited access to CAR-T therapy has the potential to widen already existing disparities in leukemia outcomes. Through the Consortium for Pediatric Cellular Immunotherapy (CPCI), we conducted a multicenter retrospective cohort study to describe the sociodemographic characteristics of pediatric and AYA patients enrolled in CAR-T clinical trials and to compare these characteristics with those of other patients with r/r B-ALL treated at these sites. We hypothesized that patients referred from an external hospital to a CPCI site and enrolled in a CAR-T trial were disproportionally non-Hispanic White and English-speaking, from higher SES areas, and traveled farther to receive care compared with the patients referred and enrolled internally.

METHODS

Study Setting

We conducted this multicenter retrospective cohort study through the CPCI. The CPCI was established to accelerate access to pediatric immunotherapy trials for the treatment of life-threatening disorders (https://www.iths.org/cpci/). In addition to the consortium's efforts related to optimizing good manufacturing practices, protocol review, and correlative studies, the CPCI Patient Advocacy Committee aims to ensure equitable enrollment in future cellular therapy clinical trials with input from patients and their families.

The CPCI includes 5 sites: Seattle Children's Hospital, University of California San Francisco Benioff Children's Hospitals, Children's Hospital of Los Angeles, Children's Hospital of Colorado, and Children's National Medical Center in Washington, DC. Data were collected following approval by the Institutional Review Board at each site.

Participant Eligibility and Cohorts

We included patients with r/r B-ALL age 0 to 27 years who were treated at 1 of the consortium sites between 2012 and 2018. This period was chosen to capture access to early-phase CAR-T clinical trials prior to more widespread use of commercial CAR-T products. Patients who enrolled but resided outside the United States were excluded. Cases were identified via the tumor registry at each site. Patients were categorized based on whether they received care primarily at a CPCI site or whether they were referred from an external hospital to a CPCI site and enrolled in a CAR-T clinical trial (including NCT01683279, NCT02028455, NCT03186118, NCT03244306, NCT0333691, NCT02435849, and NCT02625480). Patients who were treated primarily at a CPCI site were categorized by enrollment in a CAR-T clinical trial. Consortium site investigators and research staff reviewed medical records from all cases identified to verify eligibility.

Demographic and Clinical Data

Patients' demographic and clinical data were abstracted from the electronic health record (EHR) and entered in a central REDCap electronic database [22] hosted at the University of Washington Institute of Translational Health Sciences. Demographic data included age at initial diagnosis, sex, race, ethnicity, and primary language (English, Spanish, or other). Race and ethnicity were based on data collected in the EHR. Race was categorized as White, Black or African American, Asian, Native Hawaiian or Pacific Islander, American Indian or Alaskan Native, other, or unknown. Ethnicity was categorized as Hispanic, non-Hispanic, or unknown. Race and ethnicity were combined to create a composite variable (categorized as Hispanic, non-Hispanic White, non-Hispanic Black, Non-Hispanic Asian, Non-Hispanic other or multiracial, and unknown); patients with unknown ethnicity but known race were included in the appropriate race category. We present proportions of the sample by all available race and ethnicity categories, but our analysis is limited to Hispanic and Non-Hispanic White owing to sample sizes. Clinical data included years of B-ALL diagnosis and relapse, enrollment at diagnosis and/or relapse in a therapeutic clinical trial, enrollment in a CAR-T trial, and receipt of CAR-T therapy. Driving distance in miles between patient residential address and both primary oncology hospital and CAR-T therapy site were determined using Google Maps.

Measures of SES

Health insurance was categorized as private, public (Medicaid), or other/unknown. Patient home address was used to determine census tract. The ESRI ArcGIS Neighborhood Socioeconomic Status (NSES) Index uses data from the US Census Bureau 2011 to 2015 American Community Survey to assign an SES score [23,24] based on neighborhood median household income, percentage of individuals with income below the Federal Poverty Line, educational attainment of adults (age $\geq$25 years), rate of unemployment, and percentage of households with children age $<$18 that are female-headed [25]. Scores range from 0 to 100, with a score of 50 representing the national average.

Statistical Analysis

Demographic data were summarized descriptively using count and percentage for categorical variables and mean with standard deviation or median with interquartile range (IQR) for continuous variables. Patients were categorized based on whether they received treatment primarily at a CPCI site or were referred to a CPCI site from an external hospital, and among those treated primarily at a CPCI site, patients were also categorized based on enrollment in a CAR-T trial. Because each participating consortium site serves a unique geographic area with regionally varying demographics, we explored site-level variation among the 3 highest-enrolling CPCI sites (which contributed >75% of patients). For visualization, boxplots by site were constructed to illustrate the differences in SES and distance traveled within and between institutions. Comparisons of categorical variables were made using the chi-square or Fisher exact tests (if any expected cell counts were <5). Continuous data were assessed for normality using histograms and Q-Q plots. Continuous variables were compared using the *t* test if normally distributed (ie, age, SES score) and the Mann-Whitney *U* test if non-normally distributed (ie, miles to treatment center). Owing to the exploratory nature of this study, P values were not corrected for multiple comparisons. All statistical analyses were conducted using SAS 9.4 (SAS Institute, Cary, NC).

RESULTS

We evaluated 337 patients with r/r B-ALL (Figure 1), of whom 44% were Hispanic, 36% were non-Hispanic White, 2% were non-Hispanic Black, 5% were non-Hispanic Asian, 10% were non-Hispanic other or multiracial, and 4% were of unknown race or ethnicity (Table 1). Nearly 80% identified English as their primary language, and 52% of all patients had public insurance. Two hundred and twenty-five patients were treated primarily at a CPCI site; of these, 148 (66%) were not enrolled in a CAR-T trial (CPCI no CAR-T group), and 77 (34%) were enrolled in a CAR-T trial at their home institution (CPCI CAR-T group). An additional 112 patients with r/r disease were referred from an external hospital to a CPCI site and enrolled in a CAR-T clinical trial (external CAR-T group). Among Hispanic patients, 19.5% of external CAR-T patients, 37.2% of CPCI CAR-T patients, and 60.3% of CPCI no CAR-T patients had a preferred language of Spanish ($P < .01$) (Supplementary Table S1). Twelve patients who were enrolled in CAR-T trials were ultimately unable to receive cells; 10 of these patients were referred from an external hospital.

Among patients treated at CPCI sites, we compared those enrolled in CAR-T trials (CPCI CAR-T) and those not enrolled (CPCI no CAR-T) and found similar proportions of Hispanic patients (56% versus 43%), Spanish-speaking patients (22% versus 27%), and patients with public insurance (65% versus 56%) (Table 2). Patients enrolled in CAR-T trials lived closer to the CPCI center (CPCI CAR-T: 20 miles [IQR, 11 to 51 miles]; CPCI no CAR-T: 33 miles [IQR, 14 to 76 miles]; $P = .016$). At the site level, this distance gap was also evident at 2 of the 3 largest-enrolling sites (Figure 2). Within each site, SES scores were similar between groups. We did not find a consistent relationship between SES score and distance traveled to care (Supplementary Figures S1 and S2). Fewer CPCI CAR-T patients had participated in upfront therapeutic trials compared to CPCI no CAR-T patients (42% versus 59%; $P = .018$).

Table 1
Demographic Characteristics of All Patients (N = 337)

Characteristic	Value
Female sex, n (%)	139 (41.2)
Age at initial diagnosis, yr, mean (SD)	8.4 (6.3)
Race/ethnicity, n (%)	
Hispanic	147 (43.6)
NH White	120 (35.6)
NH Black	8 (2.4)
NH Asian	15 (4.5)
NH other or multiracial	35 (10.4)
Unknown	12 (3.6)
Language, n (%)	
English	269 (79.8)
Spanish	66 (19.6)
Other	2 (.6)
Insurance, n (%)	
Private	138 (40.9)
Medicaid	176 (52.2)
Other/unknown	23 (6.8)
Participation in upfront therapeutic protocol, n (%)	170 (50.4)
Miles from home (primary hospital), median (IQR)	26 (12-68)
Miles from home (CAR-T center, if received), median (IQR)	154 (23-817)
SES score, mean (range)	51.6 (11.5-90.9)
Site, n (%)	
CHLA	59 (17.5)
UCSF	41 (12.2)
Colorado	70 (20.8)
Children's National	31 (9.2)
Seattle	136 (40.4)

NH indicates non-Hispanic; CHLA, Children's Hospital of Los Angeles; UCSF, University of California, San Francisco.

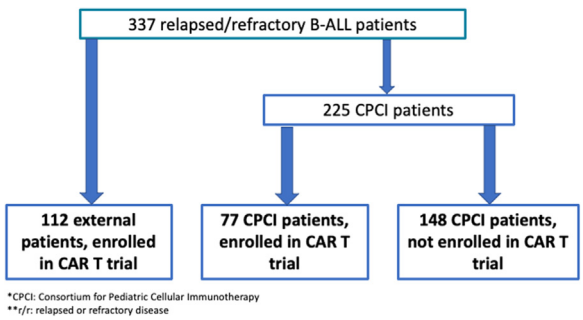

Figure 1. Participant cohorts.

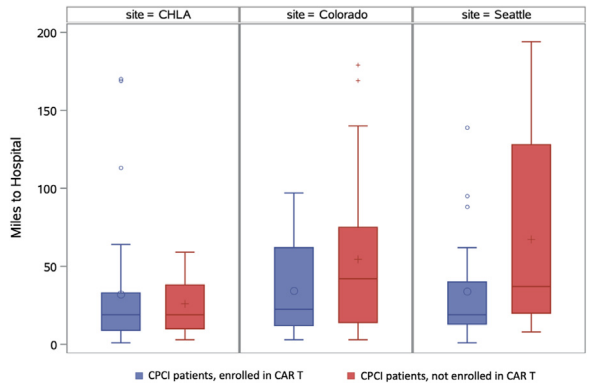

Figure 2. Distance to hospital among CPCI patients, by site and enrollment in CAR-T trial.

Table 2
Demographic Characteristics of CPCI Patients, by CAR-T Trial Participation

Characteristic	CPCI Patients Enrolled in CAR-T (N = 77)	CPCI Patients Not Enrolled in CAR-T (N = 148)	*P* Value
Female sex, n (%)	37 (48.1)	68 (45.9)	.7639
Age at initial diagnosis, yr, mean (SD)	8.9 (6.2)	8.5 (6.0)	
Race/ethnicity, n (%)			.1327
Hispanic	43 (55.8)	63 (42.6)	
NH White	22 (28.6)	49 (33.1)	
Other or unknown	12 (15.6)	36 (24.3)	
Language, n (%)			
English	60 (77.9)	106 (71.6)	.4487
Spanish	17 (22.1)	40 (27.0)	
Other	0 (0)	2 (1.4)	
Insurance, n (%)			.4151
Private	24 (31.2)	56 (37.8)	
Medicaid	50 (64.9)	83 (56.1)	
Other/unknown	3 (3.9)	9 (6.1)	
Participation in upfront therapeutic protocol, n (%)	32 (41.6)	87 (58.8)	.0179
Miles from home, median (IQR)	20.0 (11.0-51.0)	33.0 (14.0-76.0)	.0157
SES score, mean (range)	51 (12.0-90.9)	51 (11.5-81.5)	.9094
Site, n (%)			
CHLA	35 (45.5)	21 (14.2)	
UCSF	6 (7.8)	26 (17.6)	
Colorado	12 (15.6)	33 (22.3)	
Children's National	2 (2.6)	24 (16.2)	
Seattle	22 (28.6)	44 (29.7)	

A comparison of patients referred from an external hospital to a CPCI site and enrolled in a CAR-T clinical trial (external CAR-T) with CPCI CAR-T patients revealed a significantly lower proportion of Hispanic patients in the external CAR-T group (37% versus 56%; $P = .03$) (Table 3). This also was noted in site-level analyses at 2 of the 3 highest-enrolling CPCI sites (Supplementary Table S2). The external CAR-T group had lower proportions of Spanish-speaking patients (8% versus 22%; $P = .006$) and female patients (30% versus 48%; $P = .013$), as well as a significantly lower proportion of publicly insured patients (38% versus 65%; $P = .001$). Neighborhood SES scores were similar in the external CAR-T and CPCI CAR-T groups. As

Table 3
Demographic Characteristics of External and CPCI CAR-T Patients

Characteristic	External Patients Enrolled in CAR-T (N = 112)	CPCI Patients Enrolled in CAR-T (N = 77)	*P* Value
Female sex, n (%)	34 (30.4)	37 (48.1)	.0136
Age at initial diagnosis, yr, mean (SD)	7.8 (6.7)	8.9 (6.2)	.2590
Race/ethnicity, n (%)			.0300
Hispanic	41 (36.6)	43 (55.8)	
NH White	49 (43.8)	22 (28.6)	
Other or unknown	22 (19.6)	12 (15.6)	
Language, n (%)			
English	103 (92.0)	60 (77.9)	.0059
Spanish	9 (8.0)	17 (22.1)	
Other	0 (0)	0 (0)	
Insurance, n (%)			.0014
Private	58 (51.8)	24 (31.2)	
Medicaid	43 (38.4)	50 (64.9)	
Other/unknown	11 (9.8)	3 (3.9)	
Participation in upfront therapeutic protocol, n (%)	51 (45.5)	32 (41.6)	.6420
Miles from home, median (IQR)	498 (212-1669)	20.0 (11.0-51.0)	<.0001
SES score, mean (range)	53 (19.4-85.4)	51 (12.0-90.9)	.4935
Site, n (%)			
CHLA	3 (2.7)	35 (45.5)	
UCSF	9 (8.0)	6 (7.8)	
Colorado	25 (22.3)	12 (15.6)	
Children's National	5 (4.5)	2 (2.6)	
Seattle	70 (62.5)	22 (28.6)	

would be expected, distance from home differed substantially between these 2 groups, with a median distance of 498 miles (IQR, 212 to 1669 miles) for the external CAR-T group and 20 miles (IQR, 11 to 51 miles) for the CPCI CAR-T group ($P < .0001$).

DISCUSSION

Racial and ethnic minority patients with cancer are less likely to enroll on clinical trials [26–28]. Disparities in access to CAR-T therapy have been reported in adult racial and ethnic minority patients: among patients with B cell lymphoma, multiple myeloma, and ALL, Black patients were less likely to receive CAR-T therapy, and both Black and Hispanic patients were underrepresented on CAR-T clinical trials [19,26]. Additionally, patients, families, and providers have reported speaking a primary language other than English as a major barrier to clinical trial enrollment [27–29]. However, among patients with r/r B-ALL treated primarily at CPCI sites, we found similar proportions of Hispanic patients and Spanish-speaking patients among those enrolled in a CAR-T trial and those not enrolled in a CAR-T trial, suggesting equitable enrollment among those receiving treatment primarily at CAR-T therapy centers. Compared with a recent Children's Oncology Group study of relapsed B-ALL patients (AALL1331), in which 12% of participants were Black [30], our study population had a smaller number of Black patients (2%), and we were not able to meaningfully evaluate disparities by race. However, this small number of Black patients is in itself concerning, given that CAR-T trial populations should ensure appropriate representation of racial and ethnic groups so that trial results are generalizable to the diverse populations affected by B-ALL. As the indications for CAR-T therapy continue to expand, the lack of representation of Black patients on clinical trials demands thoughtful attention in future clinical trial designs.

Travel has been previously cited by patients as a barrier to enrolling in clinical trials [31,32]. The additional requirements of a CAR-T clinical trial of nearby residence for several weeks after cell infusion may add complexities for families when considering enrolling in a trial at a site distant from home. We found that among patients treated primarily at CPCI sites, those enrolled in a CAR-T trial traveled shorter distances to care compared to those not enrolled in a CAR-T trial, reinforcing the idea that distance may be a barrier to accessing these trials. Although the median distance differed by only 13 miles, this extra distance in busy metropolitan areas with high traffic burden (where the CPCI sites are located) may represent considerably more travel time and can impact transportation costs, time off work, and time away from other children. In site-level analyses, the difference in distance traveled was especially notable at Seattle Children's Hospital and Children's Hospital of Colorado, sites with large multistate catchment areas where travel and relocation to the CPCI site to participate in a CAR-T trial can be challenging.

When evaluating patients referred from external institutions for CAR-T trials, we found that Hispanic patients were underrepresented in referrals from external institutions compared to CPCI patients enrolled in CAR-T trials. This is notable given that several studies have demonstrated worse survival rates for Hispanic patients with B-ALL [5,7-9], and this underrepresentation among an already high-risk population could exacerbate outcome disparities. Furthermore, Spanish-speaking patients also were underrepresented among patients referred from external institutions, and our findings highlight that even independent of ethnic disparities in referral, there may be disparities for patients with a preferred language other than English. Families who prefer a language other than English face multiple barriers in communicating with their medical team [33], and the logistics of traveling to a new site for complex care such as CAR-T therapy may be more difficult to navigate in another language without adequate support from the healthcare system. Although there were no significant differences in enrollment in CAR-T trials between patients treated primarily at CPCI sites, underrepresentation of Hispanic patients and Spanish-speaking patients in external referrals suggests that travel to an external site may be too significant of a barrier for some patients from disadvantaged backgrounds to overcome. Additionally, low health literacy has been associated with decreased likelihood of enrolling on clinical trials [34], and thus incorporation of a direct measure of health literacy into future studies may help identify a mechanism underlying the disparities that we describe here. Finally, provider referral is an important and necessary step in this process, and external providers may have considered additional factors aside from medical eligibility when considering who to refer to CAR-T clinical trials.

In children with ALL, low SES as measured by both individual-level and area-level measures is associated with an increased risk of mortality [35]. Contrary to our hypothesis, we found that NSES score did not differ significantly between groups. Notably, SES score in our study was based on a composite measure of NSES rather than on household-level or self-reported data. Previous pediatric ALL studies also have examined the effect of insurance as a proxy for SES [10,11]. Lack of insurance is often cited as a measure of access to care in adult patients with cancer, but lack of insurance is significantly less common among patients with pediatric cancer. However, because many US children qualify for Medicaid based on household income, insurance status is often used as a proxy for household income. In our study, a lower proportion of patients with public insurance were referred from external hospitals and enrolled in CAR-T trials compared to CPCI patients enrolled in CAR-T trials (31% versus 65%; $P < .001$).

Travel to a CAR-T center incurs additional costs beyond the medical cost of therapy. Families with lower household income often lack the financial reserves needed to buffer the expenses associated with travel to receive treatment away from home. Additional factors, such as time away from work, loss of income, and care of other children, can contribute to financial stress when away from home for care [36–38]. A large retrospective analysis of adult CAR-T patients found that nearly one-third lived >2 hours away from the treating center; the majority of these patients were from higher SES neighborhoods, suggesting that the ancillary costs of treatment away from home may represent too large of a burden for patients from lower SES neighborhoods [19]. In contrast to these findings, we did not find a clear pattern across sites between SES scores and distance traveled to care among patients in our study. Economic disparity may have been difficult to identify not only because of how SES was measured in our study, but also because of the baseline variability in SES scores between sites and within each respective catchment area.

Our findings raise concerns about inequitable access to CAR-T clinical trials. Pediatric oncology care is regionalized, with care often delivered at large cancer centers. Clinical trial enrollment, particularly in the setting of r/r disease, is a pivotal component of therapy in pediatric oncology. New therapies are typically offered solely via clinical trials and at limited geographic sites; for patients who must travel great distances to access these trials, the intersectionality of rurality, low socioeconomic status, and limited English proficiency might make

these trials inaccessible. Underenrollment of racial and ethnic minority patients in clinical trials may be due in part to misalignment between open study sites and residence of these populations [39]. Our study findings are strengthened by the diversity of the populations served by the CPCI sites, and future approaches should consider matching the distribution of trial sites with the incidence of disease in diverse racial and ethnic groups. Furthermore, the key period of early therapy development is represented by our cohort of r/r B-ALL patients treated between 2012 and 2018, during which CAR-T therapy was an emerging, novel therapy. Outside referring providers might have been unaware of open trials; thus, patients may not have been readily referred to the limited trial sites owing to lack of awareness. It is also plausible that providers might have considered travel to an external site to be an excessive barrier for some families and thus may not have referred these patients. Our data suggest that within CAR-T centers, there might not be an implicit referral bias, as providers may be more familiar both with available trials at their institutions and with available resources to overcome patient barriers. Establishing partnerships between CAR-T centers and local hospital sites may help improve provider familiarity, patient referral, and patient access to CAR-T clinical trials.

Fortunately, over time, CAR-T therapy is becoming more widely available as more CAR-T products have been commercially approved and incorporated into a Children's Oncology Group clinical trial (NCT03876769). Clinicians also may be more inclined to refer patients with r/r B-ALL for CAR-T therapy as their awareness and familiarity with cellular therapy increase. However, commercial CAR-T therapies are associated with significant financial costs and are still geographically limited to certain sites [40,41]. Without dedicated attention and intervention, these disparities likely will persist for this and other novel treatments in pediatric oncology that are offered at limited sites, such as CAR-T therapy for solid tumors, meta-iodobenzylguanidine therapy, proton radiation, and phase I/II clinical trials. Expanding the geographic availability of these therapies may improve access for children with cancer from all backgrounds.

As we consider how the structure of care impacts access, we must acknowledge the role of structural racism. Patients of color may face potentially unique and unaddressed barriers, such as distance to health care centers, financial burden of traveling away from home, and implicit bias from the referring team, in accessing CAR-T therapy. Although SES is often investigated as a factor in racial disparities, race and SES are deeply intertwined, and the pervasive effects of structural racism contribute to socioeconomic, racial, and ethnic disparities.

To our knowledge, this is the first multicenter study to describe the sociodemographic characteristics of pediatric and AYA patients enrolling in CAR-T clinical trials. The findings of this study should be interpreted in the context of several limitations. SES was measured using a composite area-based measure, and area-based measures may be subject to misclassification and do not accurately reflect individual SES [42,43]. Although public insurance is often used as a proxy for low household income [10,11], public insurance also can lead to additional barriers to receiving care out of state. Race and ethnicity were identified from the EHR rather than by self-report. Additionally, the intersectionality of multiple realms of inequality (ie, ethnicity, language, insurance) can have a multiplicative effect, and we were unable to assess for possible effect modification among these groups.

Importantly, we were unable to assess the demographics of the patients treated at external institutions who were not referred for CAR-T therapy, and thus were unable to compare the sociodemographic characteristics of eligible patients who may not have been referred for these trials and those who were referred. Furthermore, 3 consortium centers accounted for the majority of patients, with 1 center having a significant external referral base. The distribution of patients within the consortium highlights how CAR-T therapy is unevenly distributed, with single centers responsible for a majority of therapy delivery, making patient access challenging. Notably, CAR-T therapy is only one of many treatment options for r/r B-ALL, and choice of therapy may be driven by provider-level and center-level practice variation, both of which may contribute to disparities in CAR-T trial enrollment. Although our findings suggest that the burden of travel and distance to care may pose significant barriers for some patients, we did not directly assess other barriers in this study; additional studies are ongoing to specifically evaluate both patient-level and provider-level barriers and to identify resources and educational opportunities to overcome barriers.

Despite these limitations, our findings are important in demonstrating that Hispanic patients, Spanish-speaking patients, and those with public insurance represent a smaller proportion of referrals from external hospital sites for CAR-T therapy compared to patients treated locally at the 5 CPCI institutions. Given the already inferior outcomes that Hispanic patients and patients from impoverished environments experience, future work must determine how to equitably offer novel therapies such as CAR-T therapy to all patients who might benefit from them. As new pediatric oncology treatments continue to emerge, we must ensure that new therapies are equitably accessible so as to not widen the gap for our most vulnerable patients.

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SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.jtct.2023.03.022.

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