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Racial Disparities in Children, Adolescents, and Young Adults with Hodgkin Lymphoma Enrolled in the New York State Medicaid Program

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Background: We examined the impact of race/ethnicity and age on survival in a publicly insured cohort of children and adolescent/young adults (AYA; 15–39 years) with Hodgkin lymphoma, adjusting for chemotherapy using linked Medicaid claims.
Materials and Methods: We identified 1231 Medicaid-insured patients <1–39 years diagnosed with classical Hodgkin lymphoma between 2005 and 2015, in the New York State Cancer Registry. Chemotherapy regimens were based on contemporary therapeutic regimens. Cox proportional hazards regression models quantified associations of patient, disease, and treatment variables with overall survival (OS) and disease-specific survival (DSS), and are presented as hazard ratios (HR) with confidence intervals (95% CIs).
Results: At median follow-up of 6.6 years, $N = 1108$ (90%) patients were alive; 5-year OS was 92% in children <15 years. In multivariable models, Black (vs. White) patients had 1.6-fold increased risk of death (HR: 1.58, 95% CI: 1.02–2.46; $p = 0.042$). Stage III/IV (vs. I/II) was associated with 1.9-fold increased risk of death (HR: 1.86, 95% CI: 1.25–2.78; $p = 0.002$) and treatment at a non-National Cancer Institute (NCI) affiliate was associated with worse DSS (HR: 2.71, 95% CI: 1.47–4.98; $p = 0.001$).
Conclusions: In this Medicaid-insured cohort of children and AYAs with Hodgkin lymphoma, Black race/ethnicity remained associated with inferior OS in multivariable models adjusted for disease, demographic, and treatment data. Further work is needed to identify dimensions of health care access not mediated by insurance, as findings suggest additional factors are contributing to observed cancer disparities in vulnerable pediatric and AYA populations.

Keywords: Hodgkin lymphoma, AYA, disparities, race/ethnicity, pediatric, Medicaid

Introduction

Hodgkin lymphoma (HL) is one of the most treatable cancers affecting children and adolescent/young adults (AYA; 15–39 years).[1,2] Despite a 5-year overall survival (OS) rate near 95%, however, inferior outcomes are reported in AYAs (vs. children), and in non-Hispanic Black (NHB) and Hispanic versus non-Hispanic White (NHW) patients.[3–5] In HL, being diagnosed at an early stage, receiving care at a National Cancer Institute (NCI) or Children's Oncology Group (COG)-affiliated cancer center (CC),[6] and enrolling on consortium clinical trials are each associated with favorable outcomes. Unfortunately, both population-level and single-center studies have demonstrated that compared with NHW children, NHB and Hispanic children and AYAs with HL are 20% more likely to present with advanced stage,[7] are 18%

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less likely to receive treatment at NCI-CC/COG centers,[8] and, despite equal risk of relapse on cooperative group clinical trials, have up to 3.5-fold increased risk of postrelapse mortality.[3]

Proposed reasons for cancer survival disparities in the United States broadly relate to either differences in disease and host biology or system-level factors influencing receipt of high-quality cancer care among minority, low-income, publicly insured pediatric and AYA populations.[9] These include, but are not limited to, under-insurance, particularly in the AYA-aged population, differences in treatment location,[6] likelihood of timely diagnosis, clinical trial enrollment, and receipt of guideline-concordant therapy.[1,3] To date, efforts to examine these factors in population-based cohorts of children and AYAs have been limited by lack of detailed information on chemotherapeutics and timing of drug administration at the individual-patient level.[10]

As a result, questions remain about the independent effects of race/ethnicity and age on HL survival both outside of the cooperative group treatment setting, and among patients who are publicly insured.[9,11] To determine whether racial/ethnic and age-related survival differences are observed after adjusting for HL therapy among a uniformly low-income cohort, we (1) examined patterns of care in a publicly insured, registry-based cohort of children and AYAs with classical HL and (2) determined the impact of race/ethnicity and age on OS and disease-specific survival (DSS), adjusting for demographic, disease, and treatment details using linked Medicaid insurance claims.

Materials and Methods

Ethical statement

This work was approved by institutional review boards (IRBs) at Columbia University Irving Medical Center and the New York State Department of Health.

Patients and cohort selection

Patients $\leq$39 years of age diagnosed with classical HL between 2005 and 2015, and enrolled in the New York State Medicaid Program (Medicaid) were identified in the New York State Cancer Registry (NYSCR). The New York State Medicaid Program insures over 6 million low-income New Yorkers. In 2010, the Affordable Care Act (ACA) introduced dependent coverage expansion, allowing individuals up to 26 years of age to maintain private health insurance coverage through their parents' employers. In New York state, additional provisions extended health insurance coverage to young adults through the age of 29, which reached many in our cohort. Among this cohort, each patient was linked to Medicaid enrollment and claims files using methods described previously.[12] Patients with lymphocyte-predominant histology, those who were HIV positive, and those who were diagnosed at autopsy or by death certificate were excluded. The final study cohort included $N = 1231$ patients for analysis (Fig. 1).

Data source and classification

Demographic information (age, sex, race, ethnicity, and place of residence) and cancer information (diagnosis date, American Joint Committee on Cancer [AJCC] stage, histology, and presence of B symptoms, including drenching night sweats, weight loss, and fevers) were obtained from the NYSCR. Age groups were built around the NCI definition of AYA (15 years as the lower threshold) and the 5-year age groupings used for population data and were categorized as $\leq$14, 15–19, 20–29, and 30–39 years. Ethnicity was categorized as Hispanic or non-Hispanic. Race was categorized as Black or African American, White or Caucasian, and Asian/Pacific islander (API). Date and cause of death were obtained from the NYS and New York City Offices of Vital Statistics, and the National Death Index for patients who died out-of-state. Information on treatment facilities was obtained from the NYSCR, Medicaid claims files, or the New York State's Statewide Planning and Research Cooperative System (SPARCS) discharge database. Treating facilities were classified as either NCI-CC or COG affiliates (for those up to 21 years), or as non-NCI/COG facilities.

Health insurance status or Medicaid enrollment category was defined in relation to HL diagnosis date, and was classified as pre-continuous, peri-continuous, pre-discontinuous, peri-discontinuous, or postdiagnosis enrollment. Pre-enrollment was defined as enrollment between 6 months and 30 days before diagnosis; peri-enrollment was defined as enrollment from 30 days before diagnosis to 2 months after diagnosis; and postenrollment was defined as over 2 months after diagnosis through 9 months after diagnosis.[13] Continuous enrollment was defined as pre- or peri-enrollment through 9 months after diagnosis without a break longer than 30 days.[13]

Treatment data. Detailed treatment data, including chemotherapy medications with dates of administration, were obtained for each patient using Medicaid insurance claims, supplemented with NYSCR data. Standard regimens used in the treatment of HL[14] were identified based on combinations of chemotherapy drugs and their relative dates of administration. Regimens analyzed individually were ABVD (adriamycin, bleomycin, vinblastine, and dacarbazine); BEACOPP (bleomycin, etoposide, adriamycin, cyclophosphamide, vincristine, procarbazine, and prednisone); ABVE-PC (adriamycin, bleomycin, vincristine, etoposide, prednisone, and cyclophosphamide); AVD (adriamycin, vinblastine, and dacarbazine); and ABV (adriamycin, bleomycin, and vinblastine).[14] Modified regimens were defined as one of these regimens administered within the expected time frame, but missing one drug. Six other standard regimens (24 patients in total) were analyzed as a group. Regimen was classified as Chemotherapy not-otherwise-specified if either (1) chemotherapy drugs and timing of infusions were administered in a pattern that did not correspond to the standard regimens or (2) specific agents were not identified in claims data, but a generic chemotherapy code was reported to the NYSCR. Patients who received one or no chemotherapy drugs were classified as having received no chemotherapy.

Statistical analyses

Descriptive statistics were calculated with χ^2 tests and are presented as frequencies and percentages. OS was measured from date of HL diagnosis to the date of death from any cause; DSS refers only to deaths from HL. Patients not known

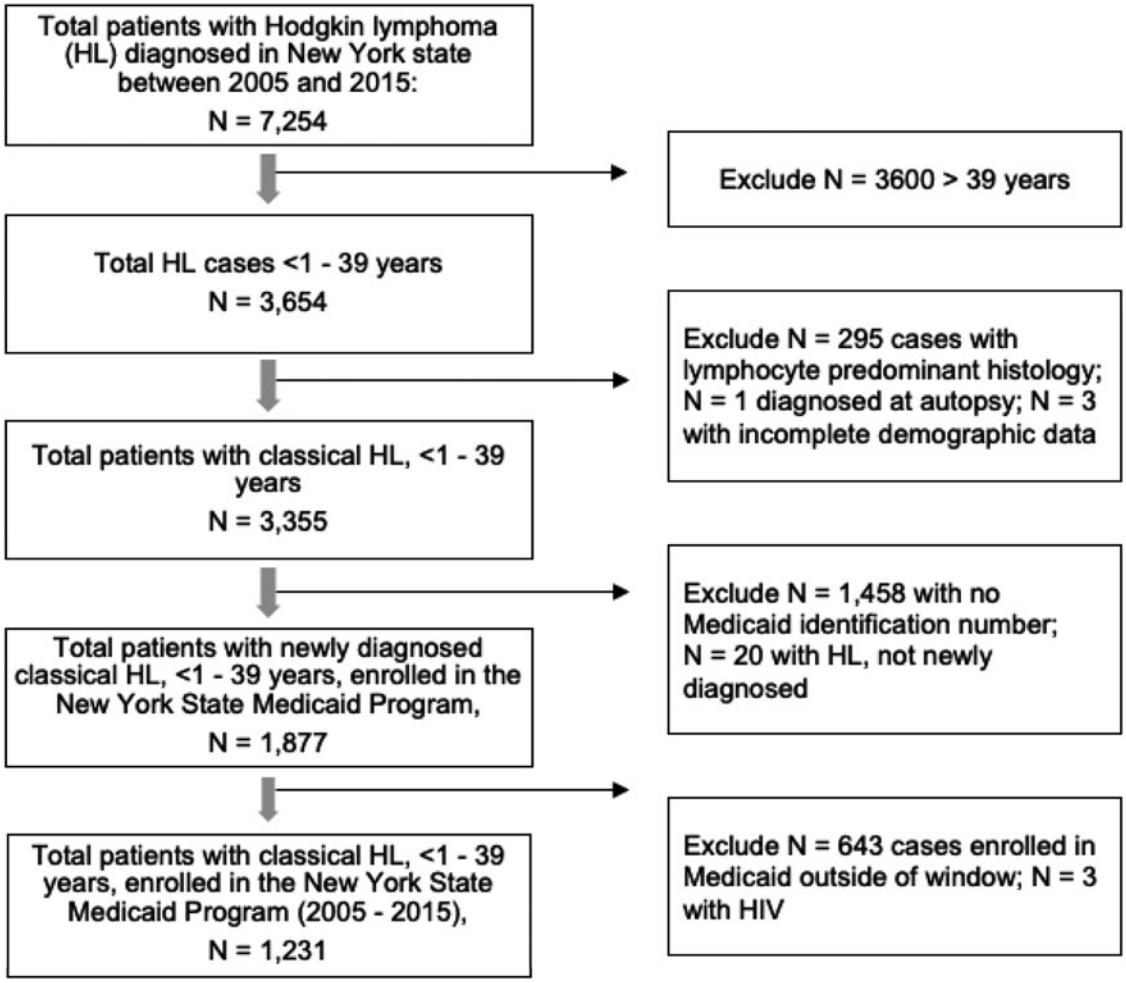

FIG. 1. Cohort selection.

to be deceased on December 31, 2017, were censored on that date. Cumulative survival probabilities were estimated using Kaplan–Meier methods and were compared across race/ethnicity and age groups using the log-rank test. Cox proportional hazards regression analyses were used to explore the relationships between race/ethnicity, age, and survival and are presented as adjusted hazard ratios (HR) with confidence intervals (95% CIs). Variables included in multivariable models were age, race/ethnicity, stage, histology, presence of B symptoms, location of care, chemotherapy regimen, radiation therapy (RT), and time period of diagnosis. Additional variables that were considered, but ultimately excluded after showing no association with outcomes included the following: timing of Medicaid enrollment (before, at, or after diagnosis), sex, distance to treatment facility, and socioeconomic status (SES) based on the neighborhood of residence. Logistic regression models examined the effects of patient and disease factors on treatment location and stage at diagnosis, and are presented as odds ratios (OR) with 95% CIs. All statistical analyses were carried out using SAS 9.4.

Results

Baseline characteristics of the full cohort ($N = 1231$) are presented in Table 1. Disease characteristics differed between children and AYAs, and between racial/ethnic groups. Compared with patients ≤ 14 years of age and those 15 years of age and older were more likely to have B symptoms at diagnosis (41% vs. 51%–58%, $p = 0.045$). Histology differed by age as well with 58% of patients ≤ 14 years of age having nodular sclerosing (NS) histology versus 75% of those 15–29 years of age, and 58% of those 30–39 years of age ($p < 0.001$). Children versus AYAs were significantly more likely to receive treatment at an NCI-CC/COG facility, and the most common chemotherapy regimen for all patients was ABVD. Finally, AYAs were significantly less likely than children to receive RT.

Between 69% and 74% of NHB and Hispanic patients (vs. 30% of NHW patients) in this cohort lived within New York City ($p < 0.001$); NHB and Hispanic patients were more likely than NHW patients to present with stage III or IV disease (51%–53% vs. 40%, $p < 0.001$). Histology differed significantly by race/ethnicity: 74% of NHW patients had NS histology versus 61%–64% of NHB and Hispanic patients ($p = 0.001$). NHB and Hispanic patients were less likely than NHW patients to receive RT (24%–25% vs. 32% $p = 0.041$) (Table 1).

At median follow-up of 6.6 years, $N = 1108$ (90%) patients were still alive. Five-year OS and DSS rates were similar between children and AYAs. Unadjusted OS, however,

Table 1. Baseline Characteristics of $N = 1,231$ Children, Adolescents, and Young Adults (<1–39 Years) Diagnosed with Classical Hodgkin Lymphoma and Enrolled in the New York State Medicaid Program (2005–2015), by Age and Race/Ethnicity

	Total	*<1–14,* N *(%)*	*15–19,* N *(%)*	*20–29,* N *(%)*	*30–39,* N *(%)*		*NH White,* N *(%)*	*NH Black,* N *(%)*	*Hispanic, N (%)*	*NH A/PI, N (%)*	
	N = *1231*	N = *93 (8)*	N = *176 (14)*	N = *598 (49)*	N = *364 (29)*	p	N = *571 (46)*	N = *276 (22)*	N = *323 (26)*	N = *61 (5)*	p
Sex											
Male	639 (52)	54 (58)	83 (47)	282 (47)	220 (60)	<0.001	299 (52)	145 (53)	163 (50)	32 (52)	0.947
Female	592 (48)	39 (42)	93 (53)	316 (53)	144 (40)		272 (48)	131 (47)	160 (50)	29 (48)	
Race/ethnicity											
NH White	571 (46)	26 (28)	79 (45)	304 (51)	162 (45)	0.005	—	—	—	—	
NH Black	276 (22)	23 (25)	36(20)	130 (22)	87 (24)		—	—	—	—	
Hispanic	323 (26)	35 (38)	53 (30)	136 (23)	99 (27)		—	—	—	—	
NH A/PI	61 (5)	9 (10)	8 (5)	28 (5)	16 (4)		—	—	—	—	
Age (years)											
<1–14	—	—	—	—	—		26 (5)	23 (8)	35 (11)	9 (15)	0.005
15–19	—	—	—	—	—		79 (14)	36 (13)	53 (16)	8 (13)	
20–29	—	—	—	—	—		304 (53)	130 (47)	136 (42)	28 (46)	
30–39	—	—	—	—	—		162 (28)	87 (32)	99 (31)	16 (26)	
Diagnosis years											
2005–2010	677 (55)	50 (54)	106 (60)	332 (56)	189 (52)	0.326	324 (57)	147 (53)	174 (54)	32 (52)	0.714
2011–2015	554 (45)	43 (46)	70 (40)	266 (44)	175 (48)		247 (43)	129 (47)	149 (46)	29 (48)	
Stage											
I/II	632 (51)	42 (45)	95 (54)	325 (54)	170 (47)	0.026	319 (56)	125 (45)	154 (48)	34 (56)	0.001
III/IV	563 (46)	51 (55)	77 (44)	250 (42)	185 (51)		230 (40)	146 (53)	164 (51)	23 (38)	
Unknown	36 (3)	0 (0)	4 (2)	23 (4)	9 (3)		22 (4)	5 (2)	5 (2)	4 (7)	
Histology											
NS	840 (68)	54 (58)	134 (76)	442 (74)	210 (58)	<0.001	425 (74)	167 (61)	207 (64)	41 (67)	0.001
MC	123 (10)	15 (16)	13 (7)	48 (8)	47 (13)		46 (8)	39 (14)	33 (10)	5 (8)	
cHL, NOS	268 (22)	24 (26)	29 (17)	108 (18)	107 (29)		100 (18)	70 (25)	83 (26)	15 (25)	
B symptoms											
Yes	643 (52)	38 (41)	89 (51)	306 (51)	210 (58)	0.045	285 (50)	152 (55)	181 (56))	25 (41)	0.045
No	486 (39)	48 (52)	76 (43)	239 (40)	123 (34)		239 (42)	95 (34)	119 (37))	33 (54)	
Unknown	102 (8)	7 (8)	11 (6)	53 (9)	31 (9)		47 (8)	29 (11)	23 (7))	3 (5)	
Region											
NYC	660 (54)	53 (57)	99 (56)	312 (52)	196 (54)	0.670	180 (32)	191 (69)	238 (74)	51 (84)	<0.001
Non-NYC	571 (46)	40 (43)	77 (44)	286 (48)	168 (46)		391 (68)	85 (31)	85 (26)	10 (16)	
Location of care											
NCI-CC/COG	589 (48)	76 (82)	114 (65)	251 (42)	148 (41)	<0.001	275 (48)	124 (45)	166 (51)	24 (39)	0.174
Community	642 (52)	17 (18)	62 (35)	347 (58)	216 (59)		296 (52)	152 (55)	157 (49)	37 (61)	
Chemotherapy regimen											
ABV	386 (3)	0 (0)	5 (3)	16 (3)	17 (5)	*	14 (2)	10 (4)	10 (3)	4 (7)	*
ABVD	690 (56)	3 (3)	50 (28)	407 (68)	230 (63)		340 (60)	150 (54)	173 (54)	27 (44)	
ABVE-PC	81 (7)	24 (26)	40 (23)	15 (3)	2 (1)		32 (6)	19 (7)	29 (9)	1 (2)	
AVD	45 (4)	2 (2)	5 (3)	21 (4)	17 (5)		21 (4)	14 (5)	8 (2)	2 (3)	
BEACOPP	35 (3)	8 (9)	8 (5)	10 (2)	9 (2)		12 (2)	7 (3)	12 (4)	4 (7)	
Chemotherapy, NOS	195 (16)	29 (31)	40 (23)	74 (12)	52 (14)		87 (15)	42 (15)	53 (16)	13 (21)	

(*continued*)

Table 1. (Continued)

	Total	*<1–14,* N (%)	*15–19,* N (%)	*20–29,* N (%)	*30–39,* N (%)		*NH White,* N (%)	*NH Black,* N (%)	*Hispanic,* N (%)	*NH A/PI,* N (%)	
	N = *1231*	N = *93 (8)*	N = *176 (14)*	N = *598 (49)*	N = *364 (29)*	p	N = *571 (46)*	N = *276 (22)*	N = *323 (26)*	N = *61 (5)*	p
Modified	79 (6)	19 (20)	19 (11)	28 (5)	13 (4)		34 (6)	16 (6)	24 (7)	5 (8)	
No chemotherapy	17 (1)	1(1)	1 (1)	5 (1)	10 (3)		8 (1)	6 (2)	1 (0)	2 (3)	
Other regimen	24 (2)	6 (6)	6 (3)	8 (1)	4 (1)		7 (1)	6 (2)	10 (3)	1 (2)	
Unknown	27 (2)	6 (6)	6 (3)	8 (1)	4 (1)		16 (3)	6 (2)	3 (1)	2 (3)	
RT											
Yes	348 (28)	45 (48)	75 (43)	163 (27)	65 (18)	<0.001	180 (32)	67 (24)	80 (25)	21 (34)	0.041
No	883 (72)	48 (52)	101 (57)	435 (73)	299 (82)		391 (68)	209 (76)	243 (75)	40 (66)	
Survival probabilities (5-year)**											
OS %	91	92	90	92	90	0.549	94	87	90	96	0.002
DSS %	95	95	95	95	94	0.853	95	93	95	98	0.199

*Not calculated because over 20% of the cells have expected counts <5.
**Estimated using Kaplan–Meier method.
ABV, adriamycin, bleomycin, vinblastine; ABVD, adriamycin, bleomycin, vinblastine, dacarbazine; ABVE-PC, adriamycin, bleomycin, vincristine, etoposide, prednisone, cyclophosphamide; AVD, adriamycin, vinblastine, dacarbazine; BEACOPP, bleomycin, etoposide, adriamycin, cyclophosphamide, vincristine, procarbazine, prednisone; cHL, NOS, classical Hodgkin lymphoma, not-otherwise-specified; DSS, disease-specific survival; MC, mixed cellularity; NCI-CC/COG, National Cancer Institute-Cancer Center/Children's Oncology Group affiliate; NH, non-Hispanic; NS, nodular sclerosing; NYC, New York City; PI, Pacific Islander; OS, overall survival; RT, radiation therapy.

differed significantly by race/ethnicity: 96% of API, 94% of NHW, 90% of Hispanic, and 87% of NHB patients were alive at 5 years ($p = 0.002$) (Table 1 and Fig. 2). In multivariable models for survival, age was not significantly associated with OS or DSS. In contrast, NHB race/ethnicity conferred a 1.6-fold increased risk of death overall (HR: 1.58, 95% CI: 1.02–2.46; $p = 0.042$) (Table 2). Disease and presenting characteristics associated with OS included advanced stage at diagnosis (HR: 1.86, 95% CI: 1.25–2.78; $p = 0.002$), and B symptoms (HR: 2.05, 95% CI: 1.31–3.23; $p = 0.002$) (Table 2). Not receiving RT was associated with an almost threefold increased risk of death from any cause (HR: 2.73, 95% CI: 1.57–4.73; $p < 0.001$), and receiving care at a non-NCI/COG center was associated with worse DSS (HR: 2.71, 95% CI: 1.47–4.97; $p = 0.001$) (Fig. 3).

In logistic regression analyses, increasing age was associated with progressively lower odds of being treated at an NCI-CC/COG facility (Table 3). In addition, those diagnosed between 2005 and 2010 were less likely to be treated at an NCI-CC/COG center compared with those diagnosed more recently. Finally, NHB and Hispanic race/ethnicity were associated with higher likelihood of stage III/IV disease (vs. I/II) at diagnosis (NHB OR: 1.62, 95% CI: 1.19–2.21; $p = 0.002$; Hispanic OR: 1.47, 95% CI: 1.09–1.98; $p = 0.013$) (Table 4).

Discussion

In this population-based cohort of over 1200 publicly insured children and AYAs with classical HL, 5-year OS and DSS were 91% and 95%, respectively. Compared to national 5-year relative survival estimates, the OS and DSS estimates in this Medicaid cohort are lower than expected in the pediatric population, and are similar to expected estimates for AYAs.[2] Our observation that NHB race/ethnicity is associated with inferior OS even after adjusting for chemotherapy regimen among a low-income population is in line with other studies that identify non-White race/ethnicity as an independent predictor of survival in oncology. In addition to NHB race/ethnicity, advanced stage, not receiving treatment at an NCI-CC/COG facility, and not receiving RT were each associated with worse survival. By age, AYAs were less likely than children to be treated at an NCI-CC/COG facility, suggesting that efforts focused on treatment location and on improving access to an NCI-CC/COG center may be a key part of addressing previously observed age-related survival differences in HL.[6] Compared to NHW patients, NHB and Hispanic children were more likely to present with advanced stage disease, which is often considered an indicator of access to primary health care.[14] These findings suggest that drivers of racial/ethnic disparities in HL may include access-related barriers that precede diagnosis,[7] while age-related survival differences may be more closely related to treatment delivery and location-of-care once diagnosis is confirmed.

As expected, chemotherapy differed by age, with >60% of AYAs ages 20–39 years receiving ABVD versus 3% of patients ≤ 14 years. In HL, use of combined-modality therapy (CMT; chemotherapy and RT) has led to substantial improvements in survival over time and is commonly recommended for younger patients with both limited and advanced stage disease.[15,16] Prior work in California found that among AYAs with HL, NHB and Hispanic patients, and those with public insurance were less likely than NHW patients to

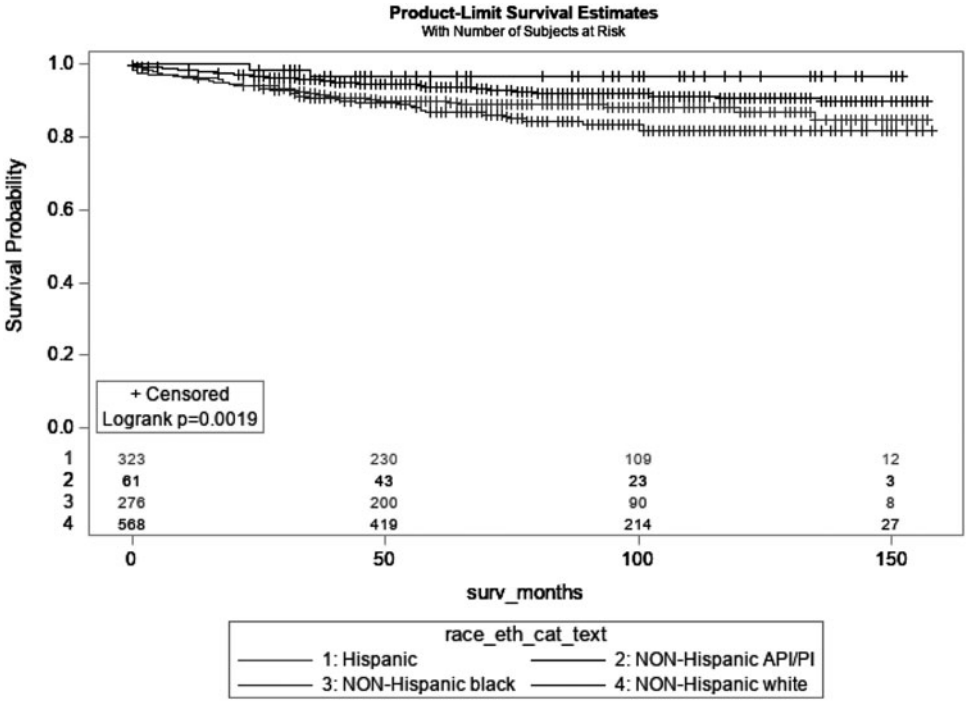

FIG. 2. Overall survival by race/ethnicity in children and AYAs with HL, enrolled in the New York State Medicaid Program. Ninety-six percent of Asian/Pacific Islanders, 94% of non-Hispanic White, 90% of Hispanic, and 87% of non-Hispanic Black patients were alive at 5 years. AYAs, adolescent/young adults.

receive CMT.[7] Similar to this analysis, not receiving RT in the California cohort was associated with worse survival. In our cohort, NHB patients were less likely than NHW patients to receive RT as part of therapy, despite being more likely to have advanced stage, and despite similar chemotherapy regimens between groups. Further work is needed to examine the reasons for racial/ethnic differences in the use of RT.

In registry analyses of pediatric and AYA cancer outcomes, studies have consistently demonstrated strong relationships between both age and survival, and race/ethnicity and survival. Few of these studies were restricted to publicly insured populations, and even fewer were able to adjust for details of chemotherapy.[17] Our findings are consistent with previous studies, with the addition of detailed chemotherapy regimen adjusted for in multivariable models. It is notable that in our patients ≤ 14 years of age, the 5-year OS rate was 92%, which is seven-percentage points lower than the national average.[18] This finding has not been previously reported in children with HL; however, in AYAs, being publicly (vs. privately)[19] insured is known to be associated with worse survival outcomes.[7,20]

Studies in pediatric and AYA oncology indicate that patients who are economically disadvantaged and publicly (vs. privately) insured[13,21] present with more advanced disease and have worse survival outcomes.[22,23] The unadjusted OS probabilities at 5 years in NHB and Hispanic patients were $\sim$7-percentage points lower than the OS probabilities in NHW patients. This finding is consistent with population-based studies demonstrating that non-White race/ethnicity is associated with inferior survival in children and AYAs with HL.[4] In an analysis of the Florida Cancer Data System registry, Grubb et al. reported significantly inferior DSS in Black vs. White children up to 21 years of age with HL (Black 74.2% vs. White 82% vs. Hispanic 82%; $p < 0.001$).[4] In a more recent study of children enrolled on COG trials for treatment of newly diagnosed HL, event-free survival did not differ in children during up-front protocol therapy, but OS was significantly lower in NHB and Hispanic patients, regardless of insurance status.[3] Our observation that children with public health insurance have worse survival than the national average supports the hypothesis that racial disparities are likely driven, at least in part, by differences in access-to-care or by other social or structural determinants of health influencing their interactions with health care systems. Although we were unable to examine detailed cause of death, the observation that NHB patients had significantly worse OS, but not DSS suggests that treatment-related toxicities, or other non-HL causes contributed to mortality in these groups.

Some of the differences in cancer-related survival are likely the result of differences in stage at presentation. In a registry analysis of 58,000 AYAs, having public or no insurance was associated with progressively higher odds of late stage at presentation for nearly all cancer sites.[7] In analyses of HL, there was a twofold increased risk of death due to advanced stage.[24] Later stage disease in HL often necessitates more intensive therapy, which, in turn, is associated with increased risk of both short- and long-term treatment-related toxicities. In this cohort, NHB and Hispanic race/ethnicity were the sole predictors of advanced stage at diagnosis, and advanced stage was associated with an 80% increased risk of death. Adjusting for stage in multivariable models, however, did not mitigate the effect of NHB race/ethnicity on survival, suggesting that they are both independent predictors of outcome in these patients. The consistent observation that Hispanic and NHB patients are more likely than NHW patients to present with advanced stage cancer, even in our Medicaid cohort, suggests that factors beyond insurance may be contributing to access-related issues in these populations.[24,25]

Table 2. Multivariable Models for Overall Survival and Disease-Specific Survival in $N=1231$ Patients <1–39 Years of age with Classical Hodgkin Lymphoma, Enrolled in the New York State Medicaid Program (2005–2015)

OS					*DSS*			
	HR	*95% CI*		p	*HR*	*95% CI*		p
Age, years (R: ≤14 years)								
15–19 years	1.41	0.57	3.47	0.461	0.71	0.20	2.57	0.604
20–29 years	0.97	0.40	2.33	0.948	0.57	0.170	1.92	0.367
30–39 years	0.85	0.35	2.08	0.726	0.43	0.1	1.50	0.186
Race/ethnicity (R: non-Hispanic White)								
Non-Hispanic Black	1.58	1.02	2.46	0.042	1.23	0.69	2.19	0.487
Hispanic	1.31	0.83	2.07	0.246	0.93	0.49	1.75	0.817
Non-Hispanic A/PI	0.41	0.1	1.72	0.224	0.29	0.04	2.15	0.225
Stage (R: I/II)								
III/IV	1.86	1.25	2.78	0.002	1.73	1.02	2.94	0.041
Unknown	0.71	0.17	3.06	0.649	0.52	0.07	4.02	0.532
Histology (R: NS)								
Mixed cellularity	1.29	0.70	2.35	0.418	1.02	0.43	2.44	0.963
cHL, NOS	1.73	1.14	2.63	0.01	1.14	0.62	2.09	0.669
B symptoms (R: no)								
Yes	2.05	1.31	3.23	0.002	1.91	1.05	3.48	0.034
Location of care: (R: NCI-CC/COG affiliate)								
Community setting	1.49	0.99	2.22	0.054	2.71	1.47	4.98	0.001
Chemotherapy regimen (R: ABVD)								
ABV	1.09	0.44	2.77	0.843	0.36	0.05	2.64	0.315
ABVE-PC	0.69	0.26	1.82	0.452	0.52	0.11	2.35	0.393
AVD	2.03	0.87	4.75	0.101	1.54	0.47	5.03	0.475
BEACOPP	0.61	0.18	2.03	0.418	0.42	0.05	3.23	0.404
Chemotherapy, NOS	0.86	0.48	1.53	0.599	0.54	0.22	1.33	0.182
Modified	1.39	0.66	2.96	0.387	1.15	0.41	3.27	0.791
Other regimens	2.94	0.99	8.69	0.051	1.27	0.160	10.13	0.820
No chemotherapy	20.77	9.19	46.93	<0.001	19.36	6.97	53.78	<0.001
Unknown	1.26	0.38	4.15	0.701	0.61	0.08	4.6	0.632
RT (R: yes)								
RT: no/unknown	2.73	1.57	4.73	0.001	2.6	1.28	5.27	0.008
Diagnosis years: (R: 2011–2015)								
2005–2010	2.41	1.54	3.79	0.001	3.07	1.61	5.86	0.001

A/PI, Asian/Pacific Islander; CI, confidence interval; HR, hazard ratio.

Numerous studies have found that for AYAs, receiving therapy at large academic cancer centers is associated with better outcomes. Using data from the California Cancer Registry, we previously reported a significant difference in likelihood of being treated at an NCI or COG center in HL patients with public vs. private insurance.[26] In this cohort, AYAs with HL were significantly less likely than children to be treated at NCI-CC/COG facilities,[6] and this, in turn, was significantly associated with worse DSS.[27] In a large cohort of children and AYAs treated for HL in California, Wolfson et al. reported that AYAs were less likely than children to receive treatment at NCI-CC/COG affiliate sites. In patients with HL, older age and non-White race/ethnicity were associated with inferior survival outcomes; however, treatment at NCI/COG facilities mitigated these disparities.[28] Although more research is needed to understand how location-of-care impacts survival, proposed hypotheses for superior outcomes at NCI-CC/COG facilities include higher clinical trial enrollment rates and access to tertiary-level supportive and post-relapse care, including stem cell transplantation and novel salvage regimens. Given our findings, in the context of prior work, efforts to improve AYA outcomes should include examining referral patterns for those with newly diagnosed HL, as well as details of supportive care at non-NCI/COG centers.

This study is subject to some limitations. We did not compare our findings to a cohort of privately insured patients, which is where we may have seen more pronounced differences by race/ethnicity and age. On the other hand, the Medicaid-based cohort has the advantage of largely controlling for socioeconomic factors that impact cancer care and treatment access in a population-based cohort. We did not have information on dose modifications or reductions, which may impact outcomes in HL, and we did not have information on disease recurrence or progression, as these data are not routinely collected by the registry. Future studies will require additional linked datasets and longer follow-up time to paint a more comprehensive picture of access, the impact of Medicaid expansion on outcomes (particularly for the AYAs), and disparities in survivorship care among these cohorts.

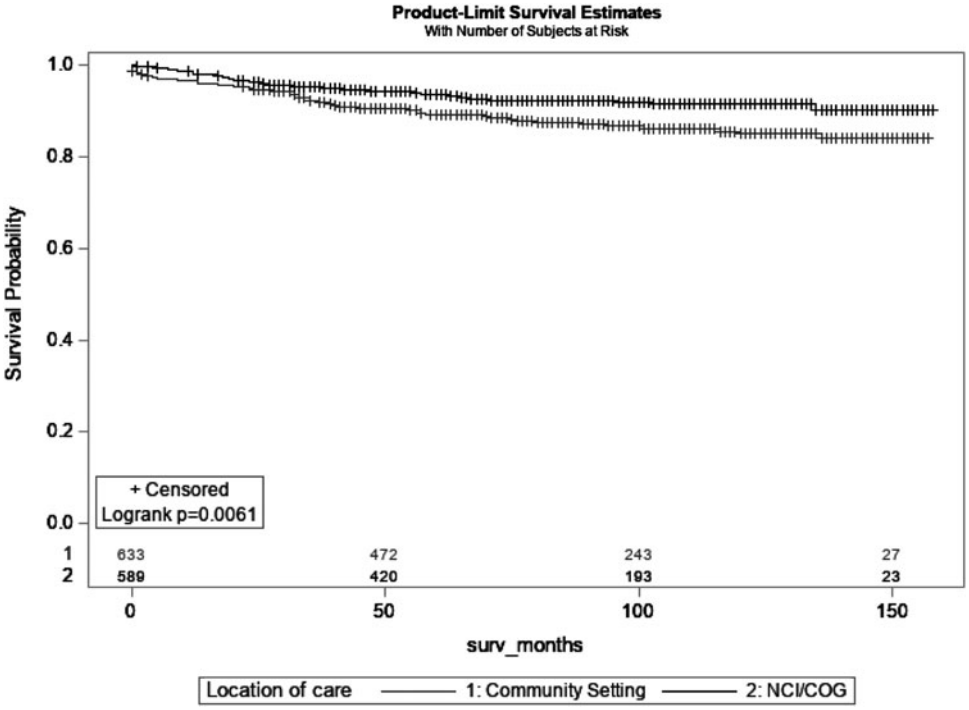

FIG. 3. Survival by location-of-care: National Cancer Institute/Children's Oncology Group Center (96% at 24 months) versus Community Center (94% at 24 months).

Conclusion

In this large cohort of publicly insured children and AYAs treated for classical HL, NHB race/ethnicity, advanced stage, and not receiving RT were each associated with higher risk of death after adjusting for chemotherapy regimen. NHB and Hispanic race/ethnicity were additionally predictive of advanced stage, a finding not unique to the HL population, and one that warrants further study. While we observed no significant difference in survival by age, AYAs were less likely than children to receive care at NCI/COG facilities, which may partly explain this population's under-enrollment in cancer clinical trials. It is notable that in our cohort of children ≤ 14 years of age with Medicaid, the OS rate at 5 years was 92%, which is almost seven-percentage points lower than the national average for patients ≤ 14 years of age with HL. This finding raises new questions about cancer and supportive care delivery in this largely low-income population, and raises concerns about the ability of safety-net health insurance to mitigate access-related inequities in pediatric and AYA oncology. Finally, the observation that NHB race/ethnicity remains significantly associated with mortality, even within a publicly insured cohort, suggests that additional factors beyond neighborhood SES or insurance status are contributing to disparities in pediatric and AYA HL.

Table 3. Predictors of Treatment at National Cancer Institute-Cancer Center/Children's Oncology Group Facility

Variable	*OR*	*95% Wald CI*		p
Age, years (R: ≤ 14 years)				
15–19 years	0.42	0.23	0.78	0.006
20–29 years	0.16	0.09	0.28	<0.001
30–39 years	0.14	0.08	0.26	<0.001
Race/ethnicity (R: non-Hispanic White)				
Non-Hispanic Black	0.82	0.59	1.13	0.222
Hispanic	1.022	0.75	1.4	0.887
Non-Hispanic A/PI	0.60	0.33	1.10	0.100
Stage (R: I/II)				
III/IV	1.08	0.85	1.38	0.516
Unknown	0.18	0.07	0.48	0.001
Region (R: New York City)				
Non-NYC	1.174	0.905	1.52	0.226
Treatment years (R: 2011–2015)				
2005–2010	0.574	0.453	0.73	<0.001

Multivariable logistic regression model of factors associated with treatment at an NCI-designated CC/COG affiliate versus community facility.
OR, odds ratio.

Table 4. Predictors of Stage III/IV Disease at Diagnosis

Variable	*OR*	*95% Wald CI*		p
Age, years (R: ≤ 14 years)				
15–19 years	0.71	0.42	1.18	0.189
20–29 years	0.69	0.44	1.09	0.115
30–39 years	0.96	0.59	1.54	0.849
Race/ethnicity (R: non-Hispanic White)				
Non-Hispanic Black	1.62	1.19	2.21	0.002
Hispanic	1.47	1.09	1.98	0.013
Non-Hispanic API	0.94	0.53	1.67	0.828
Location-of-care (R: NCI-CC/COG affiliate)				
Community setting	0.93	0.73	1.18	0.533
Region (R: New York City)				
Non-NYC (vs. NYC)	1.06	0.82	1.37	0.646
Treatment years (R: 2011–2015)				
2005–2010	0.87	0.69	1.09	0.223

Multivariable logistic regression model of factors associated with diagnosis with stage III/IV HL versus stage I/II.
API, Asian/Pacific islander.

Given the findings of this work, further analyses are needed to identify dimensions of health care access not mediated by insurance, and studies to determine why publicly insured children and AYAs with HL have worse survival than the national average are critical. Additional work is needed to elucidate why NHB patients have worse OS than Hispanic and NHW patients even after adjusting differences in presenting stage and therapy and efforts to examine referral patterns and care delivery for AYAs treated at non-NCI-CC/COG centers are warranted as well. In the interim, emphasis should be placed on the importance of early detection for all patients, referral to academic centers when possible, and close follow-up after therapy completion. For low-income AYAs and their physicians specifically, consideration of treatment location[28,29] and referrals to NCI/COG centers at diagnosis may prove a key part of improving HL outcomes overall.

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