

## Research Article

# Socioeconomic Impacts on Survival Differ by Race/Ethnicity among Adolescents and Young Adults with Non-Hodgkin's Lymphoma

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Shorter survival has been associated with low socioeconomic status (SES) among elderly non-Hodgkin's lymphoma (NHL) patients; however it remains unknown whether the same relationship holds for younger patients. We explored the California Cancer Registry (CCR), to investigate this relationship in adolescent and young adult (AYA) NHL patients diagnosed from 1996 to 2005. A case-only survival analysis was conducted to examine demographic and clinical variables hypothesized to be related to survival. Included in the final analysis were 3,489 incident NHL cases. In the multivariate analyses, all-cause mortality (ACM) was higher in individuals who had later stage at diagnosis ( $P < .05$ ) or did not receive first-course chemotherapy ( $P < .05$ ). There was also a significant gradient decrease in survival, with higher ACM at each decreasing quintile of SES ( $P < .001$ ). Overall results were similar for lymphoma-specific mortality. In the race/ethnicity stratified analyses, only non-Hispanic Whites (NHWs) had a significant SES-ACM trend ( $P < .001$ ). Reduced overall and lymphoma-specific survival was associated with lower SES in AYAs with NHL, although a significant trend was only observed for NHWs.

## 1. Introduction

Lymphomas are among the most common cancers [1] and the most common hematologic malignancy [2] in adolescents and young adults (AYAs, defined by the National Cancer Institute (NCI) as individuals aged 15–39 at diagnosis). In California, non-Hodgkin's lymphoma (NHL) represents approximately 7% of cancers diagnosed in AYAs (unpublished data). Mortality in AYA NHL patients has been found to be higher than in younger children [3, 4], attributed in part to a lack of understanding of how best to treat NHL in AYAs.

Recent attention has been given to investigating socioeconomic disparities in survival among cancer patient populations with diverse ethno-racial or socioeconomic backgrounds or with differential access to healthcare [5–10]. Concurrently, NCI—as well as several other cancer advocacy

agencies such as the Lance Armstrong Foundation—has begun to address the gaps in cancer research for AYAs [1, 11].

This study sought to examine whether socioeconomic factors beyond race/ethnicity and treatment differences influence survival in AYAs with NHL. The following research questions were investigated:

- (1) Does neighborhood-level socioeconomic status (nSES) at diagnosis predict all-cause and lymphoma-specific mortality in AYAs diagnosed with NHL, after adjustment for race/ethnicity, gender, insurance status at diagnosis, marital status, stage at diagnosis, nodality, and first-course treatment?
- (2) Is there a linear trend between decreasing nSES and shorter survival?
- (3) Is the relationship between nSES and mortality modified by race/ethnicity?

## 2. Patients and Methods

**2.1. Study Population.** A retrospective case-only analysis was performed of NHL cases diagnosed in California between 1996 and 2005 among individuals aged 15 to 39 years old using the California Cancer Registry (CCR) ( $N = 3,762$ ). The CCR, has been part of the NCI's Surveillance, Epidemiology and End Results (SEER) program since 1988 [12–15] with annual patient follow-up [16]. Data were abstracted from medical and laboratory records [14], with tumor site and histology coded using the World Health Organization (WHO) criteria in the International Classification of Diseases for Oncology (ICD-O, 3rd edition) [17]. Patient cases were selected according to ICD-O-3 coding standards and based on histologic types for nodal and extranodal NHL: SEER primary site codes 33041 and 33042. Histologic types included Burkitt's ( $n = 228$ ), diffuse large B-cell ( $n = 1,746$ ), follicular ( $n = 480$ ), lymphoblastic, ( $n = 201$ ), anaplastic large cell ( $n = 148$ ), and other types ( $n = 950$ ).

Seventy-eight cases were identified only through death certificate, obituary, or the Social Security Death Index, and an additional two were lost to follow-up. The remaining cases were identified through hospitals, inpatient/outpatient centers, oncology treatment centers, laboratories, or private practitioners.

Recorded variables in the CCR include age at diagnosis, demographic information, histology, first-course therapy (radiation, chemotherapy, and surgery status), neighborhood SES (nSES), vital status, treatment hospital type (pediatric or otherwise), and insurance status. For this analysis, health insurance status at diagnosis was categorized in one of the four following ways: (1) private insurance (including managed care, military and Veterans Administration, or other private); (2) government-funded insurance (including Medicare, Medicaid, or other state assistance programs); (3) no insurance; or (4) unknown insurance status. Individuals with government-provided insurance were not grouped with those who had private insurance because preliminary Kaplan-Meier analyses indicated that individuals with government-provided insurance had shorter survival than individuals without health insurance at diagnosis, corroborating previously published reports [18–20]. Race and ethnicity was also abstracted from patient medical records [14]. The following four categories were used in the analysis: Non-Hispanic White (NHW), Non-Hispanic Black (NHB), Hispanic/Latino (HL), and Asian/Pacific Islander (API). The nSES variable used in the CCR is a single index created from a principle component analysis of census block group-level measures of education, income, occupation, and an adjustment for cost of living, previously described [21]. Quintiles for the nSES score were included for analysis. A subgroup analysis was performed on individuals aged 18 and over at diagnosis to examine the additional predictor of marital status at diagnosis, after all other variables were included in the model.

**2.2. Cause of Death.** Cause of death was recorded according to the ICD criteria in effect at the time of death [17], using ICD-9 codes for deaths prior to 2000 and ICD-10 codes for

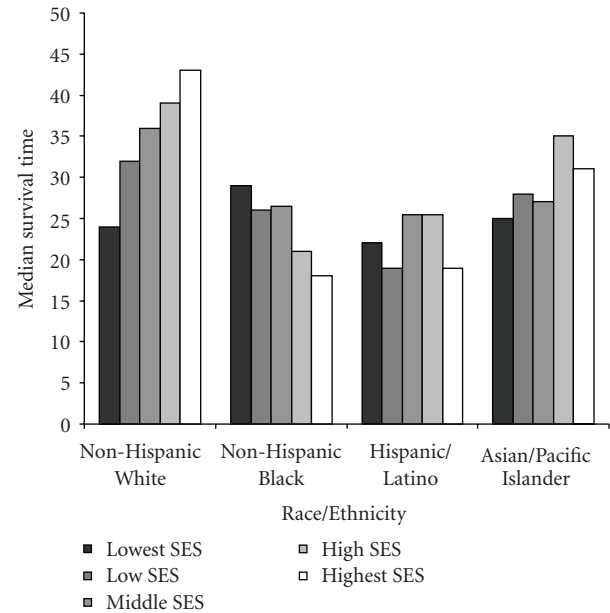


FIGURE 1: Racial/ethnic breakdown of frequency of neighborhood-level socioeconomic status (nSES).

deaths in 2000 and later. Hospital registrars contact cases annually and CCR staff review state death certificates on an annual basis to identify deceased patient cases. The last date of follow-up was the date of death or last date of contact [13].

**2.3. Statistical Analyses.** Demographic characteristics and clinical parameters were analyzed using Pearson's  $\chi^2$  tests. Kaplan-Meier curves were generated for age group, race/ethnicity, nSES categories, and insurance status and were compared with the log-rank test. Cox proportional hazard regression was performed to generate adjusted hazard ratios (HRs) for all-cause mortality (ACM) and lymphoma-specific mortality (LSM) using SAS 9.1 (SAS Institute, Inc., Cary, NC), controlling for age at diagnosis, race/ethnicity, histology, stage at diagnosis, nSES, insurance status, gender, and diagnostic year. Statistical significance was assumed for a two-tailed  $P = .05$ .

## 3. Results

**3.1. Demographic Data.** A total of 2,432 males and 1,330 females in California aged 15–39 at diagnosis with NHL between 1996 and 2005 comprised the study group. Table 1 presents distributions of demographic, clinical, and socioeconomic characteristics by race/ethnicity. There was significant variation in age, tumor staging, nodality, first-course chemotherapy, radiation, nSES, and health insurance. The majority of the cases (all histologic types) were diagnosed at a late stage, but significantly more ( $P < .01$ ) Non-Hispanic Black (52%) than Asian/Pacific Islander (34.7%) patients were diagnosed at a distant stage.

Figure 1 presents the frequencies of nSES at diagnosis by race/ethnicity and shows that for NHWs and APIs, more individuals resided in higher SES areas, while for NHBs and

TABLE 1: Demographic and clinical characteristics of adolescents and young adults diagnosed with non-Hodgkin's lymphoma<sup>a</sup>.

Characteristic	Non-Hispanic White <i>n</i> = 1,930 <i>n</i> (%)	Non-Hispanic Black <i>n</i> = 281 <i>n</i> (%)	Hispanic/ Latino <i>n</i> = 1,131 <i>n</i> (%)	Asian/Pacific Islander <i>n</i> = 380 <i>n</i> (%)	Other <i>n</i> = 40 <i>n</i> (%)	Total <i>N</i> = 3,762	<i>P</i>
Age at Diagnosis							
15–29	613 (31.8)	108 (38.4)	461 (40.8)	168 (44.2)	10 (25)	1360 (36.2)	<.0001
30–39	1317 (68.2)	173 (61.6)	670 (59.2)	212 (55.8)	30 (75)	2402 (63.9)	
Mean Age (SD)	31.5 (6.5)	30.5 (6.7)	30.2 (6.7)	29.4 (7.0)	32.4 (6.4)	30.8 (6.6)	
Year of Diagnosis							
1996–2000	1022 (53)	138 (49.1)	530 (46.9)	173 (45.5)	16 (40)	1879 (50.0)	.0031
2001–2005	908 (47)	143 (50.9)	601 (53.1)	207 (54.5)	24 (60)	1883 (50.0)	
Gender							
Male	1265 (65.5)	181 (64.4)	741 (65.5)	222 (58.4)	23 (57.5)	2432 (64.7)	.078
Female	665 (34.5)	100 (35.6)	390 (34.5)	158 (41.6)	17 (42.5)	1330 (35.4)	
Tumor stage							
Local	553 (28.7)	69 (24.6)	346 (30.6)	141 (37.1)	18 (45)	1127 (30.0)	<.0001
Regional	372 (19.3)	47 (16.7)	202 (17.9)	89 (23.4)	4 (10)	714 (19.0)	
Distant	905 (46.9)	146 (52)	526 (46.5)	132 (34.7)	10 (25)	1719 (45.7)	
Unknown	100 (5.2)	19 (6.8)	57 (5)	18 (4.7)	8 (20)	202 (5.4)	
Nodality							
Nodal	1384 (71.7)	187 (66.5)	729 (64.5)	227 (59.7)	19 (47.5)	2546 (67.7)	<.0001
Extranodal	546 (28.3)	94 (33.5)	402 (35.5)	153 (40.3)	21 (52.5)	1216 (32.3)	
First-course Chemotherapy							
Yes	1560 (80.8)	229 (81.5)	946 (83.6)	302 (79.5)	21 (52.5)	3058 (81.3)	<.0001
No	343 (17.8)	51 (18.1)	175 (15.5)	74 (19.5)	19 (47.5)	662 (17.6)	
Unknown	27 (1.4)	1 (0.4)	10 (0.9)	4 (1.1)	—	42 (1.1)	
First-course Radiation							
Yes	669 (34.7)	89 (31.7)	317 (28)	159 (41.8)	11 (27.5)	1245 (33.1)	<.0001
No	1261 (65.3)	192 (68.3)	814 (72)	221 (58.2)	29 (72.5)	2517 (66.9)	
nSES							
Highest	548 (28.4)	20 (7.1)	95 (8.4)	132 (34.7)	16 (40)	811 (21.6)	<.0001
High	489 (25.3)	47 (16.7)	144 (12.7)	92 (24.2)	8 (20)	780 (20.7)	
Middle	425 (22)	64 (22.8)	201 (17.8)	71 (18.7)	10 (25)	771 (20.5)	
Low	302 (15.6)	76 (27)	288 (25.5)	43 (11.3)	1 (2.5)	710 (18.9)	
Lowest	166 (8.6)	74 (26.3)	403 (35.6)	42 (11.1)	5 (12.5)	690 (18.3)	
Insurance							
Managed Care or Private Insurance (including Military/Veterans Affairs)	1376 (71.3)	156 (55.5)	539 (47.7)	283 (74.5)	27 (67.5)	2381 (56.2)	<.0001
Medicaid/Medicare/ Government Assistance	333 (17.3)	84 (29.9)	356 (31.5)	54 (14.2)	4 (10)	831 (19.6)	
Not Insured	65 (3.4)	12 (4.3)	98 (8.7)	15 (3.9)	1 (2.5)	191 (4.5)	
Unknown	333 (17.3)	84 (29.9)	356 (31.5)	54 (14.2)	4 (10)	831 (19.6)	

<sup>a</sup>Source: California Cancer Registry. Individuals diagnosed between January 1, 1996 and December 31, 2005.  
Abbreviations: SD: standard deviation; nSES: neighborhood socioeconomic status.

HLs, the opposite trend was true. For the remaining survival analyses, individuals with unknown race/ethnicity, stage, or chemotherapy status were excluded ( $N = 183$ ).

**3.2. Cause of Death.** During the follow-up period through December 2005, 1,081 deaths occurred among the total 3,489 patients included in this analysis. The majority of deaths were due to lymphoma-related causes ( $N = 593$ ; ICD-9 codes: 2008, 2019, 2028, ICD-10 codes: C819, C829, C833-5, C837, C844-5, C851, C859). The second most common cause of death was human immunodeficiency virus (HIV) disease resulting in NHL ( $N = 204$ ; ICD-9 code: 042, ICD-10 codes: B21.0-3, B21.7-8); an additional 43 died due to HIV complications that led to noncancerous diseases (ICD-10 code: B227). Twenty-four others died of lymphoid leukemia (ICD-9 code: 204.0, ICD-10 codes: C91.0-5), and the remaining deaths were due to other causes ( $N = 217$ ).

**3.3. Survival Analysis.** Table 2 displays the unadjusted and adjusted hazard ratios for both all-cause mortality (ACM) and lymphoma-specific mortality (LSM) for this analysis. The estimated average HR increased by 2% (95% CI: 1.01–1.03) for every increasing year of age at diagnosis after adjustment for all other variables: gender, race/ethnicity, diagnostic year, histological subtype, nodality, stage at diagnosis, nSES, insurance status at diagnosis, and first-course treatment with chemotherapy and/or radiation. In the univariate model, NHBs and HLs appeared to have increased ACM and LSM compared to NHWs. However, after adjustment no significant differences in mortality remained between NHWs and either NHBs or HLs. Conversely, adjustment increased rather than decreased the magnitude of difference in LSM for APIs compared to NHWs.

Compared to earlier stages, later stage at diagnosis appeared to have a slightly stronger effect on ACM after adjustment (adj HR: 3.16, 95% CI: 2.63–3.81) and the adjusted HR for later stage at diagnosis remained high for LSM (adj HR: 3.14, 95% CI: 2.42–4.06). Extranodal involvement appeared to increase risk of overall death, but only after adjustment (adj HR: 1.29, 95% CI: 1.11–1.50). For LSM, extranodal involvement appeared to have a protective effect (HR: 0.71, 95% CI: 0.59–0.86), but there was almost no effect after adjustment (adj HR: 0.99, 95% CI: 0.81–1.22).

Not having received chemotherapy as a first-course treatment appeared protective in the unadjusted ACM analysis (HR: 0.75, 95% CI: 0.62–0.91), but in the full model conferred shorter ACM (adj HR: 1.27, 95% CI: 1.02–1.57). On the contrary, not having first-course chemotherapy yielded protective LSM effects for both the unadjusted (HR: 0.24, 95% CI: 0.16–0.36) and adjusted HR (adj HR: 0.37, 95% CI 0.24–0.57). Results were stratified by stage at diagnosis, and it appears that only in patients with distant-staged NHL was adjusted ACM significantly higher than in patients that did not receive first-course chemotherapy (adj HR: 1.69, 95% CI 1.28–2.24). For patients who did not receive first-course chemotherapy, LSM was improved both in those with localized disease (adj HR: 0.16, 95% CI 0.07–0.38) and those with regional disease (adj HR: 0.11, 95%

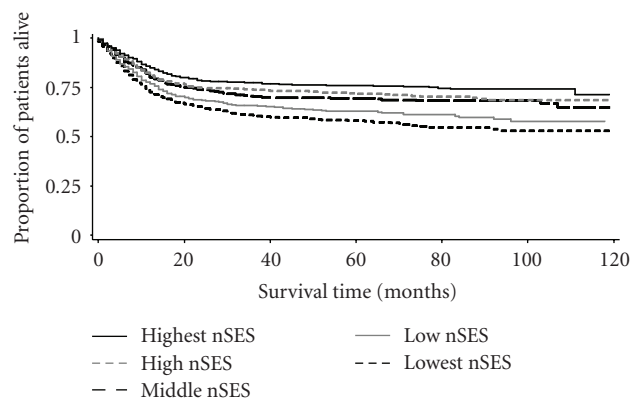


FIGURE 2: Unadjusted Kaplan-Meier survival curves ( $N = 3,489$ ) by neighborhood-level socioeconomic status (nSES).

CI 0.01–0.76). Not receiving first-course radiation therapy yielded significantly worse hazard ratios for the unadjusted ACM (HR: 1.31, 95% CI 1.15–1.50) and LSM (HR: 1.43, 95% CI: 1.19–1.71) estimates, but did not have a significant effect after adjustment.

The effects of decreasing nSES on ACM and LSM significantly worsened with every decreasing quintile both before and after adjustment, with the strongest effects evident at the lowest quintile ( $P < .05$ ) (see Figure 2 for overall unadjusted Kaplan-Meier survival curves). The adjusted hazard ratio for ACM for those residing in the poorest SES quintile at diagnosis compared to the wealthiest was 1.40 (95% CI: 1.13–1.75). All-cause mortality was higher for individuals with government-provided insurance as compared to having no insurance (HR: 1.41, 95% CI: 1.07–1.87), but after adjustment the effect was only marginally significant (adj HR: 1.32, 95% CI: 1.00–1.75). For individuals with private insurance, unadjusted survival was longer (HR: 0.62, 95% CI: 0.47–0.82) compared to those without insurance, although the difference was not significant after adjustment.

A subgroup analysis was conducted to examine whether marital status, as a means of social support, conferred longer survival among individuals aged 18 and over at diagnosis. After adjustment for the other demographic and clinical parameters in the full model, individuals who were married at diagnosis had 23% lower ACM (adj HR: 0.67, 95% CI: 0.58–0.78) as compared to those who were single, separated, divorced, or widowed at diagnosis. There was no significant difference in lymphoma-specific survival for individuals who were married at diagnosis, as compared to other marital statuses (adj HR: 1.00, 95% CI: 0.83–1.20).

**3.4. Race/Ethnicity-Specific Multivariate Survival Analysis.** Overall survival analysis was next stratified by the four racial/ethnic groups: NHW, NHB, HL, and API (Table 3). In the stratified analysis, a one-year difference in age conferred a significant survival effect only in NHWs (adj HR: 1.02, 95% CI: 1.01–1.04) and HLs (adj HR: 1.02, 95% CI: 1.01–1.04); however, the analyses may have been underpowered for NHBs and APIs. Later stage at diagnosis continued to be the strongest predictor of mortality across all age groups.

TABLE 2: Multivariate hazard ratios<sup>a</sup> for all-cause mortality<sup>b</sup> and lymphoma-specific mortality<sup>c</sup> using Cox Proportional Hazards model for adolescent and young adult non-Hodgkin's lymphoma patients.

Characteristic	ACM		LSM	
	Unadjusted HR (95% CI)	Adjusted HR (95% CI)	Unadjusted HR (95% CI)	Adjusted HR (95% CI)
Sex				
Male	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
Female	0.54 (0.47–0.63)*	0.65 (0.57–0.75)*	0.79 (0.66–0.93)*	0.93 (0.78–1.11)
Age at Diagnosis				
By year	1.01 (1.00–1.02)*	1.02 (1.01–1.03)*	0.99 (0.98–1.00)	1.00 (0.99–1.01)
Race/Ethnicity				
Non-Hispanic White	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
Non-Hispanic Black	1.50 (1.20–1.86)*	1.13 (0.90–1.41)	1.38 (1.03–1.86)*	1.11 (0.82–1.51)
Hispanic/Latino	1.30 (1.13–1.49)*	1.07 (0.92–1.25)	1.27 (1.06–1.53)	1.08 (0.88–1.32)
Asian/Pacific Islander	0.86 (0.68–1.08)	0.99 (0.78–1.26)	1.35 (1.04–1.74)*	1.52 (1.17–1.98)*
Stage				
Local	1.00 (Ref) <sup>†</sup>	1.00 (Ref) <sup>†</sup>	1.00 (Ref) <sup>†</sup>	1.00 (Ref) <sup>†</sup>
Regional	1.16 (0.93–1.45)	1.28 (1.02–1.62)*	1.85 (1.39–2.47)*	1.62 (1.21–2.18)*
Distant	2.94 (2.50–3.46)	3.16 (2.63–3.81)*	3.68 (2.91–4.65)*	3.14 (2.42–4.06)*
Nodality				
Nodal	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
Extranodal	1.03 (0.90–1.17)	1.29 (1.11–1.50)*	0.71 (0.59–0.86)*	0.99 (0.81–1.22)
First-course Chemotherapy				
Yes	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
No	0.75 (0.62–0.91)*	1.27 (1.02–1.57)*	0.24 (0.16–0.36)*	0.37 (0.24–0.57)*
First-course Radiation				
Yes	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
No	1.31 (1.15–1.50)	0.94 (0.82–1.09)	1.43 (1.19–1.71)*	1.01 (0.83–1.22)
nSES				
Highest	1.00 (Ref) <sup>†</sup>	1.00 (Ref) <sup>†</sup>	1.00 (Ref) <sup>†</sup>	1.00 (Ref) <sup>†</sup>
High	1.22 (0.98–1.50)	1.15 (0.93–1.42)	1.07 (0.81–1.41)	1.08 (0.81–1.41)
Middle	1.33 (1.08–1.63)*	1.20 (0.97–1.48)	1.27 (0.98–1.66)	1.21 (0.93–1.59)
Low	1.67 (1.37–2.05)*	1.39 (1.12–1.71)*	1.62 (1.26–2.10)*	1.49 (1.14–1.96)*
Lowest	1.97 (1.62–2.40)*	1.40 (1.13–1.75)*	1.70 (1.31–2.20)*	1.38 (1.04–1.84)*
Insurance				
None	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
Managed or Private	0.62 (0.47–0.82)*	0.82 (0.62–1.08)	0.74 (0.52–1.07)	0.96 (0.66–1.39)
Government	1.41 (1.07–1.87)*	1.32 (1.00–1.75)	1.24 (0.85–1.81)	1.16 (0.79–1.70)
Unknown	0.87 (0.63–1.21)	0.96 (0.69–1.33)	0.88 (0.57–1.37)	0.89 (0.65–1.20)

Source: California Cancer Registry. Individuals diagnosed between January 1, 1996 and December 31, 2005. Abbreviations: nSES: neighborhood socioeconomic status, ACM: all-cause mortality, LSM: lymphoma-specific mortality, HR: hazard ratio, CI: confidence interval, Ref: reference.

<sup>a</sup>All adjusted hazard ratios are fully adjusted for the other variables in the model, in addition to major histology (Burkitt's, follicular, lymphoblastic, diffuse large B-cell, anaplastic, and other/unknown) and diagnostic year. Results for individuals with race/ethnicity other than what is listed ( $N = 40$ ), or cases missing data for stage ( $N = 202$ ) or chemotherapy ( $N = 42$ ) were excluded from analysis.

<sup>b</sup>ACM:  $N = 3,489$ , with 1,081 deaths.

<sup>c</sup>LSM:  $N = 3,489$ , with 593 deaths.

\*Test for significance at  $\alpha = 0.05$ .

<sup>†</sup>Test for trend significant at  $\alpha = 0.05$ .



TABLE 3: Multivariate adjusted hazard ratios<sup>a</sup> for all-cause mortality<sup>b</sup> among race/ethnicities using Cox proportional hazards model.

Characteristic	Non-Hispanic White				Non-Hispanic Black				Hispanic/Latino				Asian/Pacific Islander			
	N	HR	95% CI		N	HR	95% CI		N	HR	95% CI		N	HR	95% CI	
Sex																
Males	1,178	1.00 <sup>†</sup> (Ref)	—		169	1.00 <sup>†</sup> (Ref)	—		701	1.00 <sup>†</sup> (Ref)	—		209	1.00 <sup>†</sup> (Ref)	—	
Females	627	0.66	0.54–0.82		92	0.77	0.48–1.23		364	0.54	0.42–0.70		149	0.73	0.45–1.20	
Age at Diagnosis																
By year	1,805	1.02	1.01–1.04		261	1.01	0.97–1.04		1,065	1.02*	1.01–1.04		358	1.02	0.99–1.05	
Tumor Stage																
Local	538	1.00 <sup>†</sup> (Ref)	—		68	1.00 <sup>†</sup> (Ref)	—		341	1.00 <sup>†</sup> (Ref)	—		139	1.00 <sup>†</sup> (Ref)	—	
Regional	367	1.21	0.86–1.71		47	0.80	0.36–1.79		202	1.46	0.99–2.16		88	1.01	0.47–2.19	
Distant	900	3.41*	2.60–4.47		146	1.89*	1.02–3.49		522	3.16*	2.28–4.39		131	3.08*	1.65–5.77	
Nodality																
Nodal	1,319	1.00 (Ref)	—		180	1.00 (Ref)	—		691	1.00 (Ref)	—		216	1.00 (Ref)	—	
Extranodal	486	1.51*	1.21–1.87		81	0.66	0.37–1.16		374	1.14	0.88–1.47		142	1.43	0.85–2.40	
First-course Chemotherapy																
Yes	1,513	1.00 (Ref)	—		222	1.00 (Ref)	—		915	1.00 (Ref)	—		295	1.00 (Ref)	—	
No	292	1.24	0.90–1.71		39	2.02*	1.09–3.71		150	1.71*	1.19–2.46		63	0.25*	0.08–0.74	
First-course Radiation																
Yes	644	1.00 (Ref)	—		86	1.00 (Ref)	—		309	1.00 (Ref)	—		155	1.00 (Ref)	—	
No	1,161	0.90	0.74–1.11		175	0.80	0.50–1.29		756	0.98	0.76–1.27		203	1.26	0.77–2.07	
nSES																
Highest	517	1.00 (Ref) <sup>†</sup>	—		18	1.00 (Ref)	—		88	1.00 (Ref)	—		125	1.00 (Ref)	—	
High	454	1.19	0.91–1.55		43	0.86	0.33–2.24		138	1.14	0.69–1.88		87	0.54	0.25–1.17	
Middle	388	1.33*	1.01–1.75		60	0.63	0.24–1.65		188	0.94	0.59–1.50		69	0.90	0.46–1.74	
Low	287	1.62*	1.22–2.14		71	0.68	0.27–1.71		273	1.06	0.68–1.64		40	1.06	0.51–2.24	
Lowest	159	2.25*	1.64–3.08		69	0.51	0.20–1.33		378	0.97	0.63–1.50		37	1.17	0.59–2.33	
Insurance																
None	61	1.00 (Ref)	—		12	1.00 (Ref)	—		93	1.00 (Ref)	—		14	1.00 (Ref)	—	
Managed or Private	1,290	0.87	0.54–1.38		144	1.65	0.38–7.11		508	0.64*	0.43–0.95		267	0.91	0.31–2.71	
Government	317	1.27	0.78–2.05		78	5.97*	1.41–25.24		340	1.00	0.68–1.47		53	1.47	0.48–4.56	
Unknown	137	0.80*	0.45–1.40		27	1.72	0.35–8.48		124	0.98	0.62–1.53		24	0.80	0.17–3.78	

Source: California Cancer Registry. Individuals diagnosed between January 1, 1996–December 31, 2005. Abbreviations: nSES: neighborhood socioeconomic status, HR: hazard ratio, CI: confidence interval, Ref: reference.

<sup>a</sup>All adjusted hazard ratios are fully adjusted for the other variables in the model, in addition to gender, major histology (Burkitt's, follicular, lymphoblastic, diffuse large B-cell, anaplastic, and other/unknown) and diagnostic year. Results for individuals with race/ethnicity other than what is listed ( $N = 40$ ), or cases missing data for stage ( $N = 202$ ) or chemotherapy ( $N = 42$ ) were excluded from analysis.

\* Test for significance at  $\alpha = 0.05$ .

<sup>†</sup> Test for trend significant at  $\alpha = 0.05$ .

Extranodal involvement was a significant adverse risk factor only for NHWs (adj HR: 1.51, 95% CI: 1.21–1.87).

Not receiving first-course chemotherapy was a significant adverse risk factor in NHBs (adj HR: 2.02, 95% CI: 1.09–3.71) and HLs (adj HR: 1.71, 95% CI: 1.19–2.46), but interestingly, a significant protective factor in APIs (adj HR: 0.25, 95% CI: 0.08–0.74). Not receiving first-course radiation therapy was not a significant hazard for any of the racial/ethnic groups. After stratification by race/ethnicity, decreasing nSES was associated with worse ACM in NHWs, with the middle (adj HR: 1.33, 95% CI: 1.01–1.75), low (adj HR: 1.62, 95% CI: 1.22–2.14), and lowest (adj HR: 2.25, 95% CI: 1.64–3.08) quintiles having significantly higher hazard of overall death than the highest. A linear trend test was significant ( $P < .001$ ). Having private insurance imparted a protective effect only for HLs (adj HR: 0.64, 95% CI: 0.43–0.95), and having government-provided insurance predicted worse ACM in NHBs (adj HR: 5.97, 95% CI: 1.41–25.24).

#### 4. Discussion

This study is one of the first to examine the impact of socioeconomic status on survival in adolescents and young adults with non-Hodgkin's lymphoma. Our analyses indicate that nSES and treatment variables attenuate much of the racial/ethnic-specific differences in survival and that, after adjustment for demographic and clinical variables, both NHBs and HLs tend to show similar survival patterns to NHWs. Asian/Pacific Islanders, however, showed significantly poorer lymphoma-specific survival than NHWs. Being married at diagnosis, a possible indicator of social support [22], as compared to being single, separated, widowed, or divorced, conferred strong protection against all-cause mortality, but not lymphoma-specific mortality.

Furthermore, when examined across racial/ethnic groups, a significant gradient in survival by nSES was only evident in NHWs. Although not significant, there was a suggestion of lower survival in APIs as nSES decreased, but the low numbers of APIs in the study likely contributed to wide confidence intervals. For HLs, having private insurance contributed to better survival, but for NHB, having government-provided insurance was associated with worse survival.

Similar findings were reported in a cohort of elderly NHL patients (age at diagnosis  $\geq 65$ ) in a study examining the association of mortality risk and SES. Over three times as many Black patients resided in the lowest SES quartile than Whites ( $P < .001$ ). The authors found increasing hazard ratios by decreasing SES quartile after adjusting for race/ethnicity, sex, age, marital status, stage, comorbidity, and therapy, and for both all-cause and NHL-specific mortality. Interestingly, individuals in the lowest SES quartile and diagnosed at stages I-II had a higher adjusted hazard ratio (adj HR: 1.31, 95% CI: 1.19–1.44) than individuals diagnosed at stages III-IV (adj HR: 1.22, 95% CI: 1.12–1.33). Finally, after controlling for disparities in stage at diagnosis and treatment, the authors failed to find significant differences in all-cause or NHL-specific mortality between Black and White patients [10].

A Brazilian study of Hodgkin's lymphoma patients also found higher mortality associated with lower SES that was unexplained by treatment regimen [23]. A Scandinavian study investigated SES influences on incidence and survival in adult NHL cases and found decreasing rates of both one- and five-year relative survival by decreasing level of education, dwelling size, and disposable income [24].

However, two other studies of SES impacts on lymphoma survival failed to find a significant association. A hospital-based study in Austria that investigated relapse-free survival (RFS) in a cohort of 218 Hodgkin's lymphoma patients (average age at diagnosis =  $35.9 \pm 15.0$  years) found that after adjustment for age survival rates actually decreased with corresponding increases in educational level and income. The authors commented that the findings seemed to be specific only to Hodgkin's patients and may partly be specific to Austria's equal-access healthcare system or to possible underlying immunological differences related to life-course exposures, such as Epstein-Barr virus positivity [25]. A study on teenaged and young adult cancer patients (aged 13–24) in England reported no gradient between survival and a composite measure of area-level poverty among NHL patients [26]. The lack of an association may be partly due to the age range included in this study; another study that examined nSES impacts on survival in leukemia patients aged 0–39 only found a significant gradient in survival among 30–39 year-olds [9].

An investigation on survival in NHL patients in Scotland and Wales found 10% and 19% shorter survival in intermediate and most deprived areas, respectively, [27]. The study used an area-level deprivation score based on four census variables (car ownership, male unemployment, overcrowding, and social class). Race and ethnicity were not reported in the Scottish study, perhaps because health research on racial/ethnic differences in survival is less widely conducted in the UK. If the study sample was fairly homogeneously Caucasian, the results would be consistent with our findings of an nSES gradient in survival among Non-Hispanic Whites.

Not finding an SES-mortality gradient in the non-White patients in our study raises several questions about the cancer experience in these populations. First, it is important to reiterate that for NHBs and HLs, although the unadjusted hazard ratios for both ACM and LSM were significantly higher than for NHWs, adjustment for the other factors in the model—including nSES, stage at diagnosis, and first-course treatment—attenuated these risks. As evident in Figure 1, there were far more NHBs and HLs residing in poorer nSES areas, which often have lower access to resources. Thus, it is possible the differences in survival by race/ethnicity commonly reported may be due more to confounding by later initiation of and poorer access to care, a phenomenon noted in Hispanic populations [28]. Measuring access to care is quite difficult, particularly in a registry-based analysis, and further studies should be done to examine why a gradient exists for NHWs but not other racial/ethnic groups. Differential access to the most effective treatment regimens may still persist for lower SES groups.

The lack of a consistent association between health insurance status and survival after adjustment was surprising, given the widely-documented increased vulnerability of patients lacking health insurance. Finding higher all-cause mortality among those with government-provided insurance compared to those without insurance suggests that there may be important disparities in access to care among Medicaid recipients. Approximately double the percentage (17.8%) of those without health insurance compared to those with government-provided health insurance (9.4%) resided in the highest nSES quintile at diagnosis. A paper analyzing the relationship of health insurance status and cancer outcomes across US demographic groups found striking disparities in cancer screening, stage at diagnosis, and survival for those uninsured or insured by Medicare or Medicaid [19]. Individuals in the general population aged 18–24 were also found to have the highest probability of lacking insurance or being insufficiently insured. Access to adequate healthcare coverage can affect cancer care, including challenges of covering premiums, deductibles, and co-payments, and difficulty remaining employed and eligible for insurance benefits [19, 29]. One study found an average increase of 13.1 weeks in wait time between diagnosis and initiation of treatment for non- or government-insured patients as compared to private health insurance, although no associations between wait times and SES, gender, age, race/ethnicity, or marital status were found [30]. These financial considerations may contribute to delays and advanced staging at diagnosis.

One of the strengths of this study is the use of CCR data with a large, heterogeneous, and population-based cohort with almost complete patient ascertainment and follow-up. Registry-based explorations of factors that contribute to longer survival are important to help identify groups that are particularly vulnerable to premature cancer mortality. Because social determinants affect health outcomes along several pathways, it is important to document the existence of persistent health disparities, particularly for understudied groups such as AYAs.

The limitations of this study include the estimation of SES based on the residence at diagnosis, which may not accurately capture some factors that contribute to healthy living environments and adequate medical care. Transitioning through developmental life stages can make AYAs a heterogeneous group; some are dependent on parents and relatives while others provide for families of their own. As such, measuring SES as a one-time neighborhood composite variable may inadequately summarize an individual patient's social and financial circumstances [31]. The way that first course of treatment is measured in the Registry is also somewhat limited; it is not possible to know the type of therapy, the dose-intensity administered, and other factors related to the treatment regimen that may have significant influence on survival. Furthermore, knowing a patient's health insurance status only at diagnosis does not reveal whether the insurance was sufficient in covering the costs associated with cancer treatment, nor does it reveal whether there were any subsequent lapses in insurance coverage. These findings do not appear to be limited to the US; however, comparability across borders may be limited due to

differing national health systems. Patient contact studies that address individual socioeconomic barriers to treatment and recovery and that can better guide potential interventions are warranted, as is the development and evaluation of programs specifically designed to meet the needs of the diverse and unique AYA population.

## 5. Conclusion

Our study is one of the first to examine socioeconomic impacts on survival in AYAs with NHL. We determined that as neighborhood SES at diagnosis increases, overall- and lymphoma-specific survival improves, after adjustment for demographic and treatment variables, and a linear trend persists. The impact of SES on mortality appeared to be independent of health insurance status at diagnosis. However, when stratified by race/ethnicity, the effects of nSES on mortality were only significant in Non-Hispanic Whites.

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