Improvements in Survival After Follicular Lymphoma by Race/Ethnicity and Socioeconomic Status: A Population-Based Study

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ABSTRACT

Purpose

A recent report suggested improvements in survival after follicular lymphoma (FL), but not for all racial/ethnic groups. To better understand the reasons for these FL survival differences, we examined the joint influences of diagnostic period, race/ethnicity, and neighborhood socioeconomic status (SES) on survival in a large population-based case series.

Methods

All patients ($n = 15,937$) diagnosed with FL between 1988 and 2005 in California were observed for vital status through November 2007. Overall and FL-specific survival were analyzed with Kaplan-Meier and Cox proportional hazards regression. Neighborhood SES was assigned from United States Census data using residence at diagnosis.

Results

Overall and FL-specific survival improved 22% and 37%, respectively, from 1988 to 1997 to 1998 to 2005, and were observed in all racial/ethnic groups. Asian/Pacific Islanders had better survival than non-Hispanic white, Hispanic, and black patients who had similar outcomes. Lower neighborhood SES was associated with worse survival in patients across all stages of disease (P for trend $< .01$). Patients with the lowest SES quintile had a 49% increased risk of death from all causes (hazard ratio [HR] = 1.49, 95% CI, 1.30 to 1.72) and 31% increased risk of death from FL (HR = 1.31; 95% CI, 1.06 to 1.60) than patients with the highest SES.

Conclusion

Evolving therapies have likely led to improvements in survival after FL. Although improvements have occurred within all racial/ethnic groups, lower neighborhood SES was significantly associated with substantially poorer survival.

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INTRODUCTION

Follicular lymphoma (FL) is the most common type of low-grade non-Hodgkin's lymphoma (NHL)¹ and comprises approximately 18% of all NHLs.^{2,3} Compared with other NHLs, FL is generally considered to be indolent and incurable, which is reflected in several characteristics of its general outcome profile. Patients with FL have longer average survival time, but are at continuous risk of relapse.⁴ At the population level, this pattern produces relative survival rates that consistently decline, rather than leveling off with increasing time after diagnosis.⁵ Although sequential treatment studies at Stanford University from 1960 to 1991 reported static survival rates,⁶ more recent clinical^{5,7-9} and population-based¹⁰ studies suggest that FL survival has improved since the mid-1970s. A possible reason for this improvement is the introduction of new

therapies like rituximab, a monoclonal antibody therapy, that was approved for the treatment of FL in late 1997 and is now used extensively.¹¹⁻¹³ In clinical studies, adding rituximab to chemotherapeutic treatment (v chemotherapeutic regimens alone) increased overall survival by 6% to 21%.^{5,9,14-16}

A recent analysis of the large Surveillance, Epidemiology, and End Results (SEER) database found that patients with FL ($n = 14,564$) diagnosed between 1990 and 1999 had a 12% decreased risk of death compared with patients diagnosed in 1983 to 1989, but that the improvements were limited to patients with advanced disease and of white race.¹⁰ What remains unclear is whether racial/ethnic differences in survival were further associated with patient socioeconomic status (SES), which portends poorer survival in studies of other cancers.¹⁷⁻¹⁹ Lower patient SES could be an important prognostic factor in FL, given that it may limit access to or

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quality of care,¹⁷ an important consideration for patients who typically experience a continuous pattern of relapse over a long period of time.⁴

With recent advances in FL therapy, it is important to determine whether improvements in survival are evenly spread across all patients or whether there are persistent disparities by race/ethnicity (as found in one recent study¹⁰), SES, or other patient characteristics. Therefore, taking advantage of a large and ethnically diverse series of patients with FL diagnosed in California from 1988 to 2005 for which neighborhood-level SES information was available, this study examined influences of patient race/ethnicity, SES, and other characteristics on overall and disease-specific survival after FL for two diagnosis periods, before (1988 through 1997) and after (1998 through 2005) the introduction of rituximab.

METHODS

Patients

Cases eligible for the study were all patients newly diagnosed with FL (International Classification of Diseases—Oncology, 3rd edition [ICD-O-3] morphology codes 9690, 9691, 9695, 9698)²⁰ in California and reported by state mandate to the California Cancer Registry during the period of January 1, 1988, through December 31, 2005. For each FL patient, we obtained California Cancer Registry information routinely abstracted from the medical record at diagnosis on age, sex, race/ethnicity, extent of disease, summary stage (localized/regional, advanced, unknown), presence of “B” symptoms (eg, night sweats, weight loss, fever), nodal status (nodal defined as ICD-O-3 sites C024, C098–C099, C111, C142, C379, C422, C770–C779; extranodal defined as all other sites), and census-block group of residence at time of diagnosis. Histologic subtype was assigned according to ICD-O-3 coding (small cleaved-cell or grade 1 [9695], mixed or grade 2 [small cleaved and large-cell; 9691], large-cell or grade 3 [9698], and FL not otherwise specified [9690]). In addition, we obtained registry information on treatment modality within 4 months after diagnosis (chemotherapy, radiation, and immunotherapy), vital status (routinely determined by the cancer registry through hospital follow-up and database linkages) as of October 2007, and, for the deceased, the underlying cause of death as coded by state vital statistics personnel. Because cancer registries generally do not collect individual-level information on patient SES, we determined the patient’s neighborhood SES for the 93% of patients whose residential census-block group at diagnosis could be geocoded using a previously described index²¹ that incorporates census measures of education, income, occupation, and cost of living. This SES index previously has demonstrated SES gradients in breast²¹ and Hodgkin’s lymphoma incidence²² and Hodgkin’s lymphoma survival.²³ Each patient with FL was assigned a neighborhood SES quintile based on the distribution of residents in California. Patients with a missing block group were randomly assigned to a block group

within their county of residence. Table 1 presents the median values of nine SES indicators, seven of which were used to generate the composite SES groups (the percentages without a high school diploma and with a college degree were not used to create the SES index, but are presented to illustrate differences in education levels).

The final study population included 15,937 patients, after exclusion, in a hierarchical manner, of those patients (1) with unknown race/ethnicity and/or age ($n = 269$); (2) of American Indian or Alaska Native ($n = 16$) race/ethnicity, as SES-specific life-tables were not available for this group; (3) with evidence of current HIV infection (on the basis of extent of disease information) or who had died of AIDS²⁴ ($n = 154$); and (4) diagnosed at autopsy, by death certificate only, or otherwise with zero or invalid survival time ($n = 47$).

Statistical Analyses

To evaluate the impact of prognostic factors, particularly diagnosis period and SES, on overall survival (OS) and disease-specific survival (DSS), we used Cox proportional hazards regression to calculate hazard ratios (HR) and associated 95% CIs. For deceased patients, survival time was measured in months from the date of diagnosis to the date of death of any cause for OS and to the date of death from NHL for DSS. Patients who died from other causes were censored at the time of death for analyses of DSS. Patients alive at the study end date (October 15, 2007) were censored at this time or at date of last follow-up (ie, last known contact); 70.9% of patients had a follow-up date within 1 year of the study end date, whereas 96.4% had follow-up within 2 years. Multivariate regression models included variables significant at $P < .15$ in univariate models or with a priori hypotheses for inclusion (eg, age, race/ethnicity, sex). All variables examined were included in the multivariate analyses, with the exception of first course of treatment as a result of its correlation with stage at diagnosis. Effect modification between neighborhood SES quintile and stage at diagnosis, histologic subtype, race/ethnicity, and sex was assessed by including interaction terms in the multivariable models and was considered present if the interaction term was significant at $P < .05$. An interaction was found between neighborhood SES quintile and stage at diagnosis, so SES findings are presented by stage at diagnosis. Additionally, regression analyses were stratified by stage at diagnosis, age, and histology, race/ethnicity, sex, histology, and stage at diagnosis, and SES to determine whether improvements in survival between the two treatment periods differed for patients in these subgroups. In all models, the proportional hazards assumption was assessed by visual inspection of the survival curves (log [–log] of the survival distribution function by log [months]); no violations of the assumption were observed. Regression analyses were conducted using SAS version 9.1 software (SAS Institute, Cary, NC). Relative survival, which adjusts for competing causes of death by comparing the observed survival of the patients in this study with their expected survival if they did not have FL, were calculated using the National Cancer Institutes’ SEER*Stat software version 6.2.4 (<http://seer.cancer.gov/seerstat>) and proprietary SES-,²¹ age-, sex-, and race/ethnicity-specific life-tables based on the 1990 and 2000 United States Census Bureau estimates for California.

Table 1. Median Value of Socioeconomic Characteristics by Index Quintile Derived by Principal Components Analysis Using 1990 United States Census Data for California Census Block Groups

Census Block Group Characteristic	Yost Socioeconomic Index Quintile				
	1 (lowest)	2	3	4	5 (highest)
Education index	11.4	12.8	13.5	14.1	14.9
Patients without high school diploma (age 25+ years), %	53.0	30.0	20.0	13.0	6.0
Patients with college degree (age 25+ years), %	4.6	11.4	18.3	26.6	45.2
Patients less than 200% poverty line, %	60.7	37.3	23.5	14.7	7.7
Blue collar workers (age 16+ years), %	80.0	72.0	67.0	59.0	46.0
Unemployed (age 16+ years in workforce), %	13.7	7.8	5.3	3.9	2.7
Median household income, \$	19,818	27,857	35,225	43,869.50	60,870.50
Median gross rent value, \$	461	546	645.50	774	980.50
Median home value, \$	89,300	127,100	169,100	224,650	352,050

Table 2. Characteristics of Patients With Incident Follicular Lymphoma by Period of Diagnosis in California

Characteristic	Period of Diagnosis				P
	1988-1997 (n = 7,935)		1998-2005 (n = 8002)		
	No.	%	No.	%	
Age at diagnosis, years					
< 65	3,942	49.7	4,154	51.9	< .01
≥ 65	3,993	50.3	3,848	48.1	
Mean	62.5		62.8		
Race/ethnicity					
NH White	6,566	82.8	6,077	75.9	< .01
NH Black	231	2.9	266	3.3	
Hispanic	842	10.6	1,164	14.6	
NH Asian/Pacific Islander	296	3.7	495	6.2	
Sex					
Male	3,873	48.8	3,979	49.7	.25
Female	4,062	51.2	4,023	50.3	
Histology					
Small cleaved cell, grade 1	3,312	41.8	2,405	30.1	< .01
Mixed, grade 2	2,445	30.8	2,124	26.5	
Large cell, grade 3	1,677	21.1	1,601	20.0	
Not otherwise specified	501	6.3	1,872	23.4	
Stage at diagnosis					
Localized/regional	3,452	43.5	3,215	40.2	< .01
Advanced	3,672	46.3	4,025	50.3	
Unknown	811	10.2	762	9.5	
B symptoms					
Present	750	9.5	1,212	15.2	< .01
Absent	2,621	33.0	4,194	52.4	
Unknown	4,564	57.5	2,596	32.4	
Nodal status					
Nodal	7,071	88.4	6,998	87.5	< .01
Extranodal	918	11.6	1,004	12.5	
Chemotherapy					
Yes	4,639	58.5	4,327	54.1	< .01
No	3,081	38.8	3,468	43.3	
Unknown	215	2.7	207	2.6	
Radiation					
Yes	1,645	20.7	1,380	17.2	< .01
No	6,290	79.3	6,622	82.8	
Immunotherapy					
Yes	141	1.8	1,052	13.1	< .01
No	7,764	97.8	6,905	86.3	
Unknown	30	0.4	45	0.6	
Vital status					
Alive	2,655	33.5	5,721	71.5	< .01
Death from NHL	3,010	37.9	1,227	15.3	
Death from HL/leukemia	117	1.5	47	0.6	
Death from other cause	1,908	24.0	645	8.1	
Death from unknown cause	245	3.1	362	4.5	
Socioeconomic status quintile					
1, lowest	873	11.0	854	10.7	.52
2	1,390	17.5	1,373	17.2	
3	1,692	21.3	1,649	20.6	
4	1,817	22.9	1,883	23.5	
5, highest	2,163	27.3	2,243	28.0	

Abbreviations: NH, non-Hispanic; NHL, non-Hodgkin's lymphoma.

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RESULTS

Table 2 shows patient demographic, tumor, and treatment characteristics for patients with FL across the two diagnostic periods. Although

most patients with FL were non-Hispanic white, the percentage of Hispanics increased 4% from 1988 through 2007 to 1998 through 2005. More than 50% of patients were in the two highest SES quintiles, and the distribution of SES was similar in the two time periods. We

also observed secular changes in data completeness, with patients more likely to be diagnosed with an unspecified histology and have the presence or absence of B symptoms recorded and secular increases in use of immunotherapy in 1998 to 2005. Between the time periods, the distributions of sex did not vary, and differences in distributions of age, stage at diagnosis, nodal status, and chemotherapy and radiation treatment were small.

Worse OS was associated with an age at diagnosis ≥ 65 years, large-cell or not otherwise specified histologic subtypes, advanced or unknown stage of disease, present or unknown B symptoms, and lower SES (SES quintile P for trend $< .01$; Table 3). On the other hand, better OS was associated with Asian/Pacific Islander race/ethnicity, female sex, and being diagnosed with FL more recently. Results were similar for DSS, with the exception of better survival also observed among those with extranodal (ν nodal) disease. Compared with patients with the highest SES, patients in the lowest neighborhood SES group had a 44% increased risk of death from all causes and 37%

increased risk of death from FL. Patients diagnosed in the most recent time period had a 22% improvement in OS and a 37% improvement in DSS. Lower SES was associated with worse OS and DSS in patients diagnosed with localized/regional (P for trend $< .01$) and advanced stage of disease (P for trend $< .01$; Table 4). Neighborhood SES was not associated with OS or DSS in patients with unknown stage of disease (data not shown). Lower SES was also associated with age younger than 65 years (P for trend $< .01$) and age ≥ 65 years (P for trend $< .01$).

From 1988 through 1997 to 1998 through 2005, OS improved for non-Hispanic whites (HR = 0.78; 95% CI, 0.73 to 0.83), blacks (HR = 0.80; 95% CI, 0.60 to 1.07), Hispanics (HR = 0.80; 95% CI, 0.68 to 0.94), and Asian/Pacific Islanders (HR = 0.65; 95% CI, 0.49 to 0.86). Somewhat stronger improvements were also found for DSS: non-Hispanic whites (HR = 0.62; 95% CI, 0.58 to 0.68), blacks (HR = 0.69; 95% CI, 0.47 to 1.02), Hispanics (HR = 0.64; 95% CI, 0.52 to 0.78), and Asian/Pacific Islanders (HR = 0.55; 95% CI, 0.38 to

Table 3. Multivariate Adjusted Hazard Ratios and 95% CI Estimates for Death From All Causes and From NHL Among Patients With FL Diagnosed Between 1988 and 2005 in the State of California

Characteristic	No. of Deaths	Overall Survival		No. of NHL-Specific Deaths	NHL-Specific Survival	
		HR	95% CI		HR	95% CI
Age at diagnosis, years						
< 65	2,601	Reference		1,696	Reference	
≥ 65	4,960	3.08	2.93 to 3.23	2,541	2.38	2.23 to 2.53
Race/ethnicity						
NH White	6,201	Reference		3,425	Reference	
NH Black	244	1.09	0.95 to 1.24	132	1.01	0.84 to 1.20
Hispanic	860	1.01	0.93 to 1.08	525	1.07	0.97 to 1.18
NH Asian/Pacific Islander	256	0.78	0.69 to 0.88	155	0.87	0.74 to 1.02
Sex						
Male	3,842	Reference		2,152	Reference	
Female	3,719	0.80	0.76 to 0.83	2,085	0.83	0.79 to 0.87
Histology						
Small cleaved cell/mixed, grades 1/2	4,988	Reference		2,848	Reference	
Large cell, grade 3	1,653	1.22	1.16 to 1.29	912	1.23	1.14 to 1.33
Not otherwise specified	920	1.24	1.16 to 1.34	477	1.14	1.03 to 1.26
Stage at diagnosis						
Localized/regional	2,836	Reference		1,298	Reference	
Advanced	3,924	1.59	1.51 to 1.67	2,546	2.09	1.95 to 2.24
Unknown	801	1.22	1.13 to 1.33	393	1.28	1.14 to 1.44
B symptoms						
Present	993	1.66	1.54 to 1.79	654	1.87	1.70 to 2.06
Absent	2,494	Reference		1,330	Reference	
Unknown	4,074	1.25	1.18 to 1.31	2,253	1.31	1.22 to 1.41
Nodal status						
Nodal	6,742	Reference		3,866	Reference	
Extranodal	819	0.92	0.85 to 0.99	371	0.82	0.74 to 0.92
Period of diagnosis						
1988-1997	5,280	Reference		3,010	Reference	
1998-2005	2,281	0.78	0.74 to 0.82	1,227	0.63	0.58 to 0.67
Neighborhood SES (quintiles)						
1, lowest	924	1.44	1.33 to 1.57	512	1.37	1.22 to 1.53
2	1,441	1.36	1.27 to 1.46	802	1.33	1.22 to 1.47
3	1,640	1.23	1.15 to 1.32	943	1.25	1.15 to 1.37
4	1,744	1.17	1.10 to 1.25	970	1.16	1.06 to 1.27
5, highest	1,812	Reference		1,010	Reference	

NOTE. Adjusted for all variables listed in the Table.

Abbreviations: NHL, non-Hodgkin's lymphoma; FL, follicular lymphoma; HR, hazard ratio; NH, non-Hispanic; SES, socioeconomic status.

Table 4. Multivariate Adjusted Hazard Ratios and 95% CI Estimates for Death From All Causes and From NHL Among Patients With FL Diagnosed Between 1988 and 2005 in the State of California by Socioeconomic Status Quintile, Stage at Diagnosis,* and Age Group at Diagnosis†

1993 and 2000 in the State of California by Socioeconomic Status, Ethnicity, Stage at Diagnosis, and Age Group at Diagnosis						
Socioeconomic Status Quintile	No. of Deaths	Overall Survival		No. of NHL-Specific Deaths	NHL-Specific Survival	
		HR	95% CI		HR	95% CI
Localized/regional stage at diagnosis						
1, lowest	317	1.49	1.30 to 1.72	142	1.31	1.06 to 1.60
2	562	1.50	1.34 to 1.68	253	1.35	1.14 to 1.60
3	631	1.33	1.19 to 1.48	296	1.28	1.09 to 1.50
4	659	1.21	1.09 to 1.35	290	1.11	0.95 to 1.30
5, highest	667	Reference		317	Reference	
Advanced stage at diagnosis						
1, lowest	505	1.46	1.30 to 1.63	329	1.48	1.28 to 1.70
2	733	1.36	1.23 to 1.50	470	1.38	1.22 to 1.56
3	846	1.24	1.13 to 1.36	570	1.32	1.17 to 1.48
4	906	1.19	1.09 to 1.31	591	1.22	1.09 to 1.37
5, highest	934	Reference		586	Reference	
Age < 65 years at diagnosis						
1, lowest	359	1.67	1.46 to 1.91	230	1.55	1.31 to 1.84
2	467	1.54	1.37 to 1.75	306	1.48	1.28 to 1.73
3	566	1.40	1.25 to 1.57	369	1.34	1.16 to 1.54
4	607	1.28	1.14 to 1.43	386	1.19	1.03 to 1.37
5, highest	602	Reference		405	Reference	
Age ≥ 65 years at diagnosis						
1, lowest	565	1.35	1.21 to 1.50	282	1.27	1.09 to 1.47
2	974	1.29	1.18 to 1.40	496	1.26	1.12 to 1.42
3	1,074	1.15	1.06 to 1.25	574	1.20	1.07 to 1.35
4	1,137	1.13	1.04 to 1.22	584	1.14	1.02 to 1.28
5, highest	1,210	Reference		605	Reference	

Abbreviations: NHL, non-Hodgkin's lymphoma; FL, follicular lymphoma; HR, hazard ratio.

*Adjusted for age at diagnosis, sex, race/ethnicity, histology, period of diagnosis, presence of B symptoms, and nodal status.

†Adjusted for sex, race/ethnicity, stage at diagnosis, histology, period of diagnosis, presence of B symptoms, and nodal status.

0.78). From 1988 through 1997 to 1998 through 2005, improvements in survival were more marked for patients younger than 65 years (HR for OS = 0.67; 95% CI, 0.61 to 0.74; HR for DSS = 0.52; 95% CI, 0.46 to 0.59) than for patients ≥ 65 years (HR for OS = 0.84; 95% CI, 0.78 to 0.89; HR for DSS = 0.70; 95% CI, 0.63 to 0.76). Furthermore, improvements in survival in the most recent diagnosis period occurred in men and women and in patients with all stages of disease, with all histologies, and in all SES quintiles (data not shown). Similarly, 5-year relative survival estimates were higher in 1988 through 1997 than 1998 through 2005 for all patient subgroups (Table 5; Fig 1).

DISCUSSION

In our population-based study of nearly 16,000 patients with FL, survival improved from 1988 through 1997 to 1998 through 2005, likely as a result of evolving therapies, particularly the introduction of rituximab in 1997.^{5,9,14-16} Even though improvements in survival over time were seen in patients of all race/ethnicities, poorer survival remained associated with lower neighborhood SES.

To our knowledge, this is the first study to consider socioeconomic disparities in FL survival; these disparities may be attributable to a number of sources, including inadequate health insurance, delayed diagnosis resulting in later stage at diagnosis, poor or delayed access to high-quality cancer treatment, or having comorbidities that influence treatment options or survival.^{17,19,25} Patients who are unin-

sured or Medicaid insured have been shown repeatedly to have poorer survival after cancer.²⁵ Our observations of SES disparities in survival among patients ≥ 65 years of age, who are overwhelmingly eligible for Medicare, make it unlikely that insurance status completely explains the differences. It also seems unlikely that differential stage at diagnosis could explain the disparities, as stage distributions were comparable across SES quintiles, and associations of neighborhood SES with OS and DSS did not vary by stage at diagnosis. Although we considered first course of treatment, we did not have a measure of treatment quality, which has been shown previously to be poorer in patients with low SES.¹⁹

Disparities could also result from patients with low SES receiving inadequate long-term follow-up or poor integrated care after cancer treatment,¹⁹ as access to and quality of treatments for relapse^{4,26} or other complications²⁷⁻³⁰ may vary by SES. Moreover, if differences in health behaviors and comorbid conditions are more prevalent in low SES patients, as found in studies of other cancers,¹⁹ or in nonwhite racial/ethnic groups,³¹⁻³³ then these factors could increase complications and reduce survival in these patients.

A limitation of this study is its use of an ecologic, neighborhood measure of patient SES. Individual-level measures of SES are not collected by United States cancer registries. Although individual-level measures associate more strongly with health outcomes than neighborhood measures,^{34,35} studies controlling for both types of SES measures have found health effects of neighborhood SES above and

Table 5. Five-Year Relative Survival by Period of Diagnosis in California

Characteristic	Period of Diagnosis			
	1988-1997		1998-2005	
	%	SE	%	SE
Overall	71.3	0.7	80.5	0.8
Age at diagnosis, years				
< 65	76.7	0.7	85.9	0.8
≥ 65	63.7	1.1	71.8	1.5
Race/ethnicity				
NH White	71.9	0.7	81.3	0.9
NH Black	67.1	3.9	73.5	4.8
Hispanic	68.4	1.9	77.4	1.9
NH Asian/Pacific Islander	70.9	3.0	84.1	2.7
Sex				
Male	69.6	0.9	78.3	1.2
Female	72.9	0.9	82.8	1.1
Histology				
Small cleaved cell, grade 1	74.6	1.0	81.9	1.4
Mixed, grade 2	73.3	1.2	82.7	1.4
Large cell, grade 3	62.8	1.5	78.4	1.8
Not otherwise specified	68.1	2.7	78.4	1.8
Stage at diagnosis				
Localized/regional	82.5	1.1	89.9	1.2
Advanced	67.0	1.2	73.5	1.1
Unknown	71.3	0.7	80.5	0.8

Abbreviation: NH, non-Hispanic.

beyond those of individual SES.^{35,36} Aside from proxying individual SES, neighborhood-level SES may influence health through the social (eg, social support, attitudes toward health), physical (eg, pollution), and built (eg, availability of health services, recreational opportunities) environments of the neighborhood.^{35,36} Our neighborhood SES measure is multifaceted, incorporating aspects of education, income, occupation, and cost of living, and has been used previously to demonstrate SES gradients in Hodgkin's lymphoma survival.²³

Our findings are consistent with a recent SEER analysis reporting a temporal improvement in survival after FL from 1978 to 1999,¹⁰ but not with its observations of improvements limited to whites (v blacks)

and patients with advanced disease.¹⁰ Prior studies including all patients with NHL also reported improvements in relative survival more for whites than blacks.^{37,38} In this study, we observed improvements in 5-year relative survival in all four racial/ethnic groups, although blacks did have the lowest rates in all comparisons.

Our population-based study design allows us to generalize our SES-related disparities in FL survival to a larger population, which is important because of previous findings of poorer average survival from population-based cancer registries than clinical trials,³⁹ probably because of the disproportionate selection of better-prognosis patients into clinical trials or superior treatment from academic cancer centers. Population-based cancer registries seem to have low levels of pathologic misclassification of patients with FL; 83% of cancer registry FL diagnoses were confirmed by expert pathology rereview,⁴⁰ and an even higher concordance (94%) was demonstrated by the International Lymphoma Study group across nine study sites worldwide.¹ Furthermore, FL classification seems to have been robust over time, as agreement of registry- and coder-assigned ICD-O-3 codes for FL ranged between 84% and 89% for the periods 1988 to 1994 and 1998 to 2000.⁴¹ Our study also uniformly collected survival time for all patients, which minimized bias owing to differential follow-up.

Because we used population-based registry data, this study was unable to include clinical prognostic information not routinely collected by cancer registries, such as serum lactate dehydrogenase and hemoglobin concentrations, thus limiting our ability to control for prognostic scores.⁴² However, we were able to adjust outcomes for available demographic and tumor characteristics. Although we considered the types of cancer-directed treatment received within 4 months of diagnosis (radiation, chemotherapy,

Fig 1. Five-year relative survival by socioeconomic status and period of diagnosis, 1988 to 1997 and 1998 to 2005, California.

and immunotherapy), we did not have details on treatment such as radiation field and dose, type of immunotherapy, or treatment received after this period. We also lacked information about treatment failure, recurrence, or other events occurring after the first 4 months of treatment. Our study was also unable to address the effects of stage migration, whereby stage classifications may be susceptible to improvements in newer imaging modalities.⁴³

Although FL survival has improved in recent years for most patients, this study shows that patients with lower neighborhood SES continue to experience substantially poorer survival, regardless of race/ethnicity, stage of diagnosis, or other sociodemographic factors, providing a strong basis for socioeconomic disparities in FL treatment and/or follow-up. In addition to specific aspects of treatment and follow-up care that may differ by region or other socioeconomic determinants, further research should seek to uncover other modifiable sources of these associations, which may include prevalence of comorbid conditions, aspects of treatment compli-

ance or other health seeking behaviors, or less likely, clinical characteristics of FL that may vary by individual-level SES.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

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