Original Article

Health Status and Quality of Life Among Non-Hodgkin Lymphoma Survivors

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BACKGROUND: A growing body of evidence suggests that long-term survivors with 1 of the more common forms of adult cancer report a quality of life (QOL) similar to that in the general population. However, specific concerns have been identified (sexual dysfunction, fatigue, distress) in this population. Also, less is known concerning survivors of adult non-Hodgkin lymphoma (NHL), a disease often marked by alternating periods of disease and remission. Therefore, in the current study, the authors compared the QOL status of individuals who reported having active NHL with the QOL status of individuals who were disease-free short-term survivors (STS) (2-4 years postdiagnosis) and long-term survivors (LTS) (≥5 years postdiagnosis). **METHODS:** Eligible survivors completed a mailed survey with validated measures, including physical and mental health status measured with the Medical Outcomes Study 36-item Short Form, cancer-related QOL, the Functional Assessment of Cancer Therapy-Lymphoma module, and self-reported impact of cancer. Other data were collected to examine as correlates. **RESULTS:** Seven hundred sixty-one survivors identified from 2 North Carolina cancer registries participated. The average survivor was 10.4 years postdiagnosis (range, 2-44 years postdiagnosis) and was age 62.7 years (range, 25-92 years). Survivors with active disease (n = 109) demonstrated worse physical and mental health functioning, worse QOL, and less positive and more negative impacts of cancer compared with disease-free survivors (n = 652; all $P \leq .01$). No significant differences were observed between STS and LTS. **CONCLUSIONS:** Although survivors with NHL who had active disease reported more negative outcomes compared with off-treatment survivors, the length of time after diagnosis did not appear to matter with regard to outcomes for STS or LTS. In addition, mixed results from comparisons with general population norms suggested the need for supportive care for this diverse survivorship group. **Cancer 2009;115:3312–23. © 2009 American Cancer Society.**

KEY WORDS: quality of life, non-Hodgkin lymphoma, post-traumatic stress, Functional Assessment of Cancer Therapy-General, Functional Assessment of Cancer Therapy-Lymphoma, Medical Outcomes Study Short Form, Impact of Cancer.

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A growing body of evidence suggests that long-term survivors who are diagnosed and treated for 1 of the more common forms of adult cancer report a quality of life (QOL) similar to that of the general population.[1-4] However, specific areas of unresolved concern have been identified in this population, including sexual dysfunction,[3,5,6] low energy level and fatigue,[1,7,8] and post-traumatic stress (PTS).[9-12] Furthermore, several studies have demonstrated positive outcomes associated with having cancer, such as greater appreciation for life, closer personal relationships, and deeper spiritual understanding (post-traumatic growth).[6]

Less is known regarding the health status and QOL specific to survivors of adult non-Hodgkin lymphoma (NHL), the sixth most common cancer in the United States. NHL is a heterogeneous group of cancers of the lymphatic system with an overall 5-year survival rate of 50% to 60% (statistics vary, depending on the cell type, stage of disease at diagnosis, and treatment). Indolent lymphomas generally carry a good prognosis with a median survival of 10 years but a high rate of recurrence, and they usually are not curable in advanced stages. Treatment for the indolent forms includes periods of watchful waiting, radiation therapy, and chemotherapy. By comparison, from 30% to 60% of individuals who convert to or who present with aggressive forms of NHL can be cured with intensive chemotherapy regimens, but the disease has a shorter natural history, and the greatest risk of recurrence is within 2 years of treatment cessation.[13] Thus, from a patient perspective, various forms of NHL are experienced as life-long, chronic illnesses with intermittent, symptom-free and symptom-exacerbation phases that require treatment.

Given the expected increase in NHL incidence rates[14] attributed to the increasing average age of the US population, the time has come to understand the health and QOL status and needs of this population overall and by survivorship status. Such information may suggest areas for treatment or the targeting of scarce healthcare resources. Thus, for this report, we used 3 outcome measures to compare the health and QOL status of individuals who reported active NHL disease with the status of individuals who were short-term survivors (STS) (2-4 years postdiagnosis) and long-term survivors (LTS) ($\geq$5 years postdiagnosis) who reported being in remission or cured.

Figure 1 illustrates the conceptual model underlying this research, which is based on coping theories[15] and empiric research.[3,9,12,16-18] Clinical (CLN) characteristics are conceptualized as stressors, whereas survivor life-course factors are comprised of selective demographic (DEM), health (HTH), and psychosocial (PSO) characteristics that may influence each other and the outcome of these stressors. For example, the quality of social support can affect an individual's appraisal of cancer's impact on his/her life,[18] which may either diminish or enhance individual coping strategies and possibly may lead to negative and/or positive QOL-related outcomes. Also, individuals with active disease may be more likely to experience higher levels of clinical stress than those who are in remission or cured.

MATERIALS AND METHODS

Participants and Procedures

Potential study participants were identified through the Duke and University of North Carolina Tumor Registries and were contacted by mail after we received Institutional Review Board and physician approvals. Patients with NHL were eligible if they were aged $\geq$19 years and 2 years postdiagnosis. Participants provided written informed consent.

Measures

Health Status and Quality-of-Life Outcomes

Three measures were used to assess outcomes. First, the Medical Outcomes Study Short Form (SF-36), a general health measure of physical and mental health functioning, was used to allow for comparisons with general population-based norms. It is comprised of 36 items representing 8 subscales and 2 summary scores, the Physical Component Score (PCS) and the Mental Component Score (MCS).[19] For purposes of comparison, a score of 50 (standard deviation [SD], 10) represents the population mean.[20] Reliability estimates ranged from $\alpha = .84$ to $\alpha = .95$. Second, to capture cancer-specific QOL, the 27-item Functional Assessment of Cancer Therapy-General (FACT-G) and the 15-item FACT-Lymphoma (FACT-LYM) module, which lists lymphoma-related symptoms (eg, fevers, night sweats, itching), were administered.[21] The FACT-G originally was intended for patients who were receiving treatment, but it is being used increasingly with off-treatment samples. Reliability statistics for both measures ranged from $\alpha = .77$ to $\alpha = .93$. Third, the Impact of Cancer (IOC) instrument was used

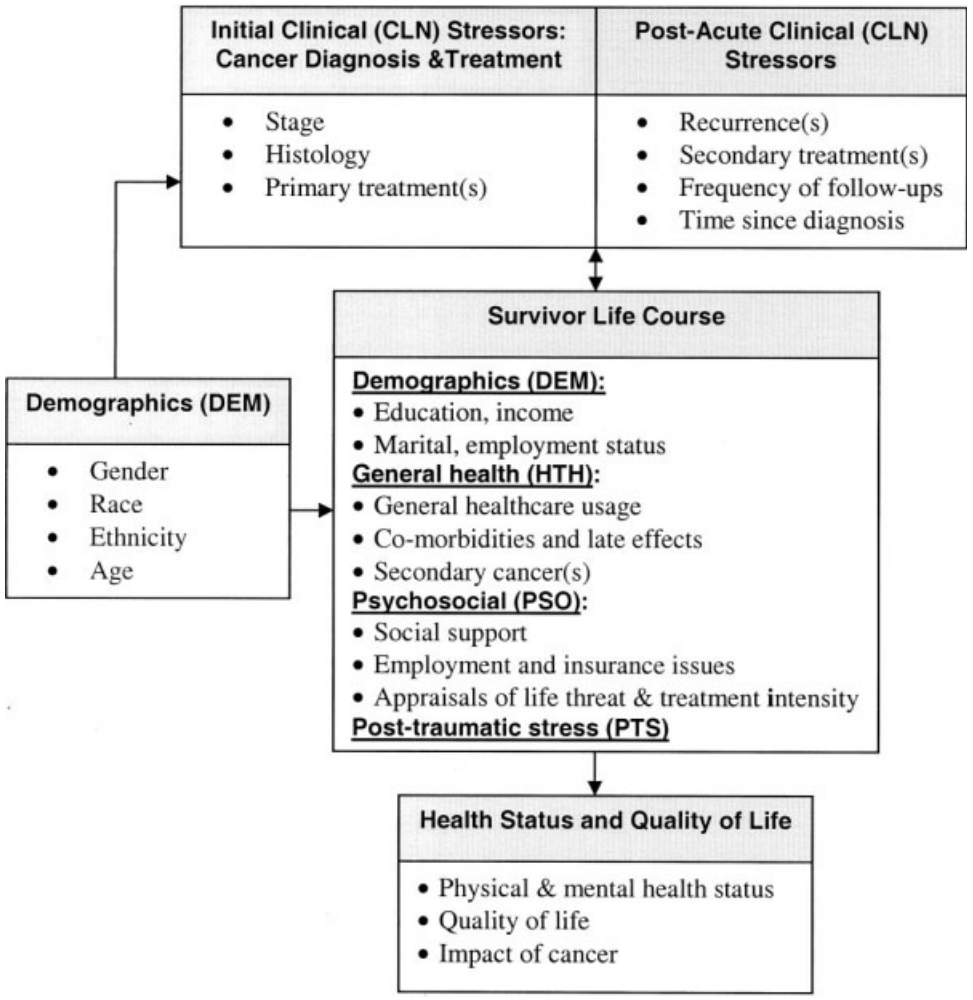

FIGURE 1. Conceptual model of cancer survivorship.

to assess respondents' perceptions of positive and negative impacts of cancer in various aspects of their lives using 5 positive subscales, 5 negative subscales, and 2 summary scores (Positive Impact and Negative Impact).[18] The IOC was developed to assess certain aspects of survivorship that were not measured by other QOL measures (eg, health worries, meaning of cancer, post-traumatic growth).[22] Reliability estimates for the IOC ranged from $\alpha = .62$ to $\alpha = .91$. Higher scores on all outcome measures indicate better health status and QOL, except for the IOC Negative Impact score, for which a higher score indicates greater negative impacts.

Demographic and Clinical Characteristics

Information on DEM variables (sex, race, ethnicity, age, income, education, marital status, employment status) and CLN variables (histology, stage, surgery, radiation therapy, chemotherapy, bone marrow/stem cell transplantation, biologic therapy, NHL treatment status, recurrence, number of oncology-related visits, site of treatment) was collected from self-reports and from tumor registry databases. NHL histology was categorized as indolent or aggressive based on the updated Revised European-American Lymphoma/World Health Organization classification.[23]

General Health

For HTH variables, the Self-administered Comorbidity Questionnaire[24] was used to assess non-NHL health problems. In addition, selected questions related to healthcare use were adapted for use from the Childhood Cancer Survivor Study survey.[25]

Table 1. Characteristics of the Study Sample (n=761)

Characteristic	All Survivors, N=761*		Active Disease, n=109†		Short-term Survivors, n=150‡		Long-term Survivors, n=502§		*P*‖
	No.	%	No.	%	No.	%	No.	%	
Demographics									
Sex									
Men	383	50.3	54	49.5	73	48.7	256	51	.868
Women	378	49.7	55	50.5	77	51.3	246	49	
Race									
Caucasian	659	86.6	88	80.7	133	88.7	438	87.3	.103
African-American	67	8.8	15	13.8	10	6.7	42	8.4	
Multiple race	27	3.5	5	4.6	5	3.3	17	3.4	
Other	8	1.1	1	0.9	2	1.3	5	0.9	
Ethnicity									
Non-Hispanic	750	98.6	107	98.2	148	98.7	495	98.6	.933
Hispanic	11	1.4	2	1.8	2	1.3	7	1.4	
Income level									
<$30,000	183	26.7	28	28	32	21.3	123	27.3	.763
$30,000-$59,999	208	30.3	32	32	39	26	137	30.4	
$60,000-$89,999	126	18.4	21	21	27	18	78	17.3	
≥$90,000	169	24.6	19	19	37	24.7	113	25.1	
Education									
≤High school	208	27.8	29	27.6	28	18.8	151	30.5	.080
Some college or trade school	236	31.6	31	27.5	55	36.9	150	30.4	
College or postgraduate	304	40.6	45	47.9	66	44.3	193	39.1	
Marital status									
Married or living together	579	76.3	81	75	122	81.3	376	75	.268
Not married or living together	180	23.7	27	25	28	18.7	125	25	
Employment status									
Retired or unemployed	450	59.8	69	63.9	80	54.1	301	60.7	.229
Employed	302	40.2	39	36.1	68	45.9	195	39.3	
Mean±SD age at enrollment, y	62.7±13.4		62.7±12.6		59.7±14.1		63.6±13.2		.008
25-49	135	17.7	20	18.3	36	24	79	15.7	.282
50-64	279	36.7	44	40.4	54	36	181	36.1	
65-79	271	35.6	34	31.2	48	32	189	37.6	
≥80	76	10	11	10.1	12	8	53	10.6	
Clinical characteristics									
NHL histology									
Indolent	361	50.2	85	81	57	40.4	219	46.3	<.001
Aggressive	358	49.8	20	19	84	59.6	254	53.7	
NHL stage at diagnosis									
I	210	31.3	29	34.1	39	28.7	142	31.6	.278
II	141	21	10	11.7	31	22.8	100	22.2	
III	131	19.5	23	27.1	26	19.1	82	18.2	
IV	189	28.2	23	27.1	40	29.4	126	28	
No. of treatment types: Mean±SD	2.1±1.1		2.4±1.3		2.2±1.1		2.1±1		.006
Surgery	226	30.5	25	22.9	44	30.6	157	32	.235
Radiation	364	47.8	48	44	61	40.7	255	50.8	.064
Chemotherapy	617	81.1	83	76.2	120	80	414	82.5	.290
Bone marrow/stem cell transplantation	119	15.6	16	14.7	28	18.7	75	14.9	.521
Biologic therapy	215	28.3	60	55.1	59	39.3	96	19.1	<.001
Current treatment status									
Not in treatment	686	90.9	38	35.5	150	100	502	100	NA
Receiving treatment	69	9.1	69	64.5	0	0	0	0	
No. of NHL recurrences									
0	517	68.6	51	47.7	120	80.5	346	69.5	<.001
≥1	237	31.4	56	52.3	29	19.5	152	30.5	
Mean±SD age at diagnosis, y	52.3±14.1		54.5±13.2		55.9±14.2		50.7±14		<.001
Range	19-87		20-82		22-87		19-82		

(Continued)

Table 1. (Continued)

Characteristic	All Survivors, N=761*		Active Disease, n=109†		Short-term Survivors, n=150‡		Long-term Survivors, n=502§		P‖
	No.	%	No.	%	No.	%	No.	%	
Mean±SD y since diagnosis	10.4±7.2		8.1±5.1		3.8±0.7		12.9±7.3		<.001
2-4	182	23.9	32	29.4	150	100			
5-9	285	37.5	48	44			237	47.2	
10-14	125	16.4	19	17.4			106	21.1	
15-19	81	10.6	6	5.5			75	15	
≥20	88	11.6	4	3.7			84	16.7	
General health									
Secondary cancer	104	13.7	16	14.8	11	7.3	77	15.4	.040
No secondary cancer	655	86.3	92	85.2	139	92.7	424	84.6	
Mean±SD no. of comorbidities	2.9±2.1		3±2.2		2.5±2.1		3±2.1		.053
Psychosocial									
Social support: Mean score±SD	83.6±15.9		81.7±16.1		85.9±14.2		83.3±16.3		.092
Range	26-100		34-100		36-100		26-100		
Mean score±SD appraisal of life threat and treatment intensity	19.4±6		19±6.5		19.1±5.9		19.5±5.8		.575
Range	6-30		6-30		6-30		6-30		
Employment and insurance issues related to cancer: Mean number of issues related to cancer±SD	1±2		1.2±2.2		1±2		1±2		.671
Range	0-17		0-12		0-11		0-17		
Post-traumatic stress									
PTSD symptom clusters: Mean number of symptom clusters±SD	0.6±0.9		0.6±0.9		0.6±0.9				.014
Range	0-3		0-3		0-3				
PTSD symptoms: Mean score±SD	26.7±9.7		26.2±8.3		26±9.3				<.001
Range	17-78		17-55		17-78				

SD indicates standard deviation; NHL, non-Hodgkin lymphoma; NA, not available; PTSD, post-traumatic stress disorder.
* Not all variables total 761 because of missing data.
† The active disease group represents individuals who self-reported current NHL.
‡ The short-term survivor group represents individuals at 2 to 4 years after diagnosis who reported that they were disease free.
§ The long-term survivor group represents individuals at ≥5 years after diagnosis who reported that they were disease free.
‖ The *P* values shown are for the overall comparison.

Psychosocial

The 20-item Medical Outcomes Study-Social Support Survey was used to measure perceived availability of social support[26] (score range, 20-100; $\alpha = .97$). The Appraisal of Life Threat and Treatment Intensity Questionnaire (6 items; score range, 6-30; $\alpha = .80$) was used to assess the extent to which cancer and its treatment were perceived as life-threatening and intense.[27] Information on employment-related and insurance-related situations and difficulties was collected using 24 questions (possible score range, 0-24, $\alpha = .82$) derived from a Cancer and Leukemia Group B research instrument.[28]

Post-traumatic Stress

The PTS Disorder (PTSD) Checklist assesses symptomatology in noncombat populations by presenting a symptom checklist that closely mirrors criteria from the Diagnostic and Statistical Manual (4th edition) for a formal diagnosis of PTSD.[29,30] The instructions were modified for the current study, such that survivors were asked to rate each symptom in the past 4 weeks with respect to their diagnosis and treatment for lymphoma. The continuous scoring method was used, and the Cronbach α ranged from .78 to .91.

Statistical Analysis

Descriptive statistics were used to estimate the health status and QOL means for this population overall and by survivorship status (active disease, STS, and LTS). Chi-square tests and analyses of variance were used to compare distributions and mean scores on outcome variables and

the covariates across the 3 survivor groups. The amount of missing data for income (10%) and disease stage (12%) variables justified multiple imputation using the Markov-chain Monte Carlo method[31]; imputed values for disease status and outcome variables were not generated.

Twenty datasets that contained imputed values were included in the multiple linear regression analyses using the SAS MIANALYZE procedure (SAS Institute, Cary, NC).[32] Multiple linear regressions were conducted to examine the association between survivorship status and outcomes, adjusting for covariates. For all comparisons, individuals with active disease were the reference group. For each of the 5 outcome summary scores (PCS, MCS, FACT-G, IOC Positive Impact, IOC Negative Impact), 6 sequential series of linear regression models were constructed to examine the association with active disease such that each domain of covariates was added in order of strength of association with the outcomes (correlations with DEM and CLN were small; correlations with HTH were medium; and correlations with PSO and PTS were large). That is, the first model tested for the relation between active disease and disease-free status with summary scores without accounting for covariates; then, subsequent models added DEM, CLN, HTH, PSO, and PTS. The order of entry had no bearing on the final results for each measure. Statistical analyses, including tests for multicollinearity, were carried out using SAS software (version 9.1; SAS Institute, Inc, Cary, NC).

RESULTS

Seven hundred sixty-one participants (74% response rate) provided informed consent. Table 1 lists the information collected by total sample and survivorship status. Sample bias analyses using demographic information from the registries indicated that participating survivors were less frequently non-white and were older at diagnosis and study enrollment than nonparticipants (all $P < .001$). Survivors who reported having active disease were more likely to be diagnosed with an indolent lymphoma, to receive biologic therapy, to have more recurrences and types of treatment, and to have PTS than disease-free survivors (all $P < .01$). STS were younger at enrollment, less likely to have a secondary cancer, and had less comorbidity than those with active disease or LTS (all $P < .05$). Although it was not detailed in Table 1, many reported receiving current treatment for comorbid conditions, including high blood pressure (34%), heart disease (17%), back pain (15%), osteoarthritis (15%), and depression (13%). Fourteen percent of survivors reported a history of other nonskin cancers, including prostate, breast, melanoma, colon, and bladder.

Bivariate Analyses

Figure 2 displays the means and SDs for the outcome variables by disease status. In terms of physical (PCS) and mental (MCS) health, survivors who had active disease demonstrated worse functioning compared with disease-free survivors (all $P \leq .01$). Those with active disease also demonstrated significantly worse QOL, as measured by the FACT-G and lymphoma-specific items, than both STS and LTS (all $P < .01$). Also, those with active disease reported significantly less positive impact and more negative impact (all $P < .01$) on the IOC than those who were disease-free. STS and LTS did not differ significantly in any of the outcomes measured. Descriptive statistics for the outcome variables and their correlations are presented in Table 2. All outcomes were related to each other significantly with the exception of the IOC Positive Impact, which was related to the MCS ($P < .05$) and lymphoma symptoms ($P < .001$) only.

Compared with general population-based norms (PCS and MCS scores: mean $\pm$ SD, 50 ± 10),[20] individuals with active disease scored lower in physical health (mean $\pm$ SD, 41.1 ± 11.9) and mental health (mean $\pm$ SD, 45.4 ± 11.5). Disease-free survivors fared better, as expected, but still seemed to have worse physical health scores (STS, mean $\pm$ SD, 47.3 ± 10.4; LTS, mean $\pm$ SD, 45.7 ± 9.9) than the general adult population.[20] However, after comparing our disease-free sample with their corresponding age-stratified normed groupings (ages 25-34 years, 35-44 years, 45-54 years, 55-64 years, 65-74 years, and $\geq$75 years), our sample scored comparably (within $\pm$1.8 points) on the PCS. Regarding mental health, scores from our disease-free survivors on the MCS (STS, mean $\pm$ SD, 50.3 ± 9.9; LTS, mean $\pm$ SD, 49.3 ± 11.4) were close to the general population norm[20]; however, our sample scored lower ($\leq$4.1 points) on the MCS than the corresponding age-stratified groups (except for the groups ages 35-44 years and $\geq$75years), with the largest difference observed between the group ages 25 years to 34 years.[20]

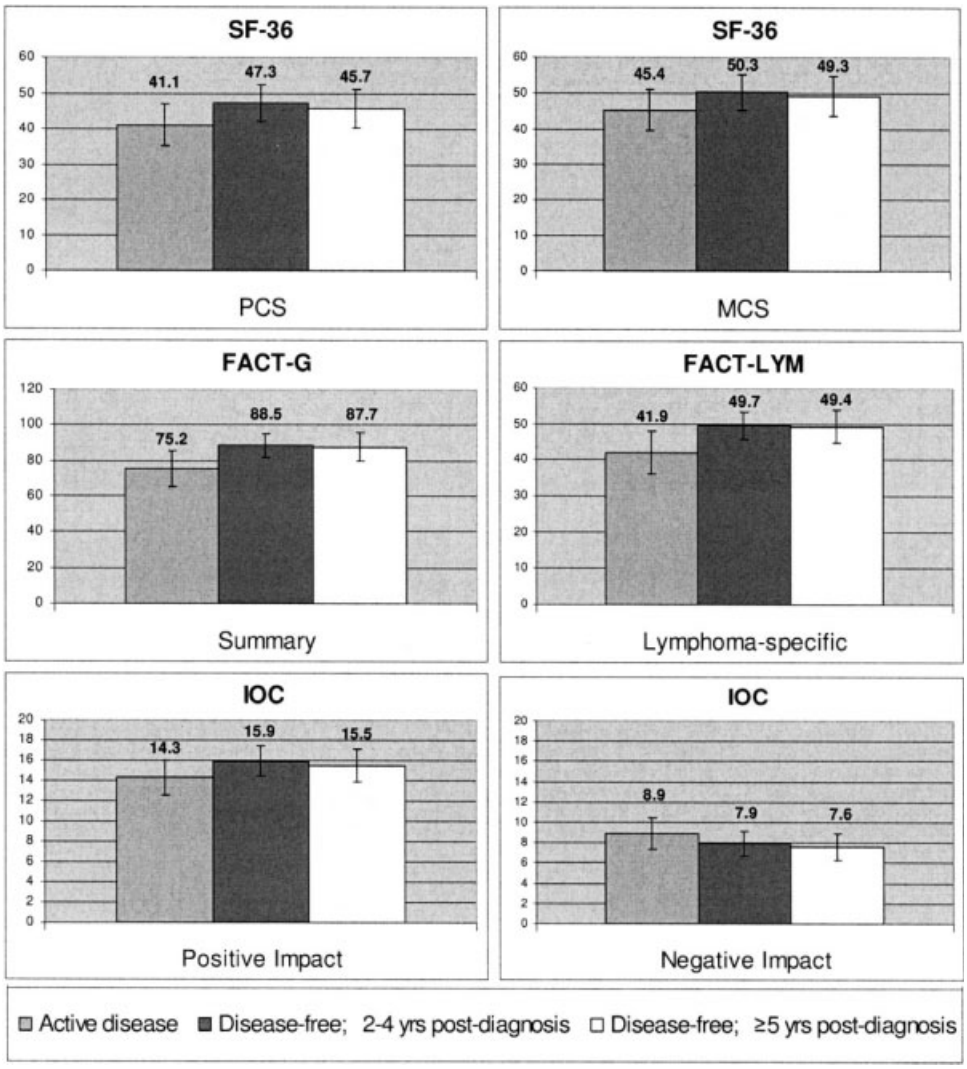

FIGURE 2. Health status and quality of life in non-Hodgkin lymphoma survivors (n = 761). Higher scores indicate better quality of life, except for the Impact of Cancer (IOC) Negative Impact; error bars represent 1 standard deviation from the mean. Comparisons between survivors with active disease and disease-free survivors were statistically significant (all $P < .01$). No statistically significant difference between short-term and long-term disease-free survivors was noted (all $P > .10$). SF-36 indicates Medical Outcomes Study-Short Form; PCS, Physical Component Summary; MCS, Mental Component Summary; FACT-G, Functional Assessment of Cancer Therapy-General; FACT-LYM, Functional Assessment of Cancer Therapy-Lymphoma.

Regression Results

Tables 3 and 4 display the regression coefficients for the relations between survivorship and health status and QOL as measured by the SF-36, FACT-G, and IOC. The coefficients for the series of 6 sequential models represent the increase in the mean level of health status and QOL related to disease-free survivorship status after adjusting for the covariates. For example, the SF-36 Model I indicates that STS and LTS scored 6.2 and 4.6 points higher, respectively, than those with active disease before adjusting for covariates ($P < .001$). Although the differences were statistically nonsignificant, LTS reported lower health status and QOL than STS in all models.

The Medical Outcomes Study Short Form

Consistent with bivariate analyses, Model I (Table 3) indicates that disease-free survivorship had a strong relation to better PCS scores ($P < .001$). However, this relation quickly became nonsignificant after accounting for the CLN covariates. In total, 48% of the variance was

Table 2. Descriptive Statistics and Correlations (n=761)

		Correlation				
Item	Mean score±SD	2	3	4	5	6
1. SF-36 PCS	45.4±11	0.23*	0.51*	0.52*	−0.06	−0.37*
2. SF-36 MCS	49±11.2		0.71*	0.63*	−0.08†	−0.56*
3. FACT-G	86.1±16.6			0.81*	−0.01	−0.72*
4. FACT-LYM symptoms	48.4±9.5				−0.14*	−0.73*
5. IOC Positive Impact	15.4±3.3					0.27*
6. IOC Negative Impact	7.8±2.8					

SD indicates standard deviation; SF-36, Medical Outcomes Study 36-item short form; PCS, Physical Component Summary; MCS, Mental Component Summary; FACT-G, Functional Assessment of Cancer Therapy-General; FACT-LYM, Functional Assessment of Cancer Therapy-Lymphoma; IOC, Impact of Cancer.
*$P < .001$.
†$P < .05$.

Table 3. Regression Coefficients for the Relation Between Survivorship Status (Active Disease Versus Disease Free) and Health Status (n=761)

	SF-36 PCS			SF-36 MCS		
Model Covariates	R^2	STS vs Active *b* (SE)	LTS vs Active *b* (SE)	R^2	STS vs Active *b* (SE)	LTS vs Active *b* (SE)
Model I. SS	.028	6.2 (2)*	4.6 (1.4)*	.018	4.9 (2)*	4.0 (1.5)†
Model II. SS+DEM	.222	4.8 (1.3)*	4.2 (1.1)*	.076	4.8 (1.4)*	3.7 (1.2)†
Model III. SS+DEM+CLN	.256	2.6 (1.9)	0.9 (1.8)	.103	7.1 (2.1)*	5.2 (2)†
Model IV. SS+DEM+CLN+HTH	.447	1.0 (1.6)	0.5 (1.5)	.184	6.1 (2)†	5 (1.9)†
Model V. SS+DEM+CLN+HTH+PSO	.459	0.7 (1.6)	0.5 (1.5)	.290	5.5 (1.9)†	5.1 (1.8)†
Model VI. SS+DEM+CLN+HTH+PSO+PTS	.480	−0.2 (1.6)	−0.7 (1.5)	.519	2.0 (1.6)	1.2 (1.5)

SF-36 indicates Medical Outcomes Study 36-item short form; PCS, Physical Component Summary; MCS, Mental Component Summary; R^2, proportion of variation in the dependent variable explained by the regression equation; STS, short-term disease-free survivor (<5 years); Active, patients who self-reported current non-Hodgkin lymphoma; *b*, unstandardized regression coefficient (slope); SE, standard error; LTS, long-term disease-free survivor (≥5 years); SS, survivorship status; DEM, demographic covariates (sex, race, ethnicity, age, income, education, marital status, employment status); CLN, clinical covariates (histology, stage, surgery, radiation therapy, chemotherapy, bone marrow/stem cell transplantation, biologic therapy, recurrence, number of oncology-related visits, site of treatment); HTH, general health covariates (other cancer [excluding skin], comorbidity, years since last physical examination); PSO, psychosocial covariates (social support, appraisal of life threat and treatment intensity, employment and insurance issues); PTS, post-traumatic stress.
*$P < .001$.
†$P < .01$.

accounted for by all covariates. Similar to the PCS, the relation between disease-free survivorship and the MCS was significant ($P < .01$). Unlike the PCS, significant differences persisted until the PTS covariate was added. A slightly higher percentage (52%) of the variance was accounted for by all covariates.

The Functional Assessment of Cancer Therapy-General

Consistent with the SF-36, Model I (Table 4) indicates that disease-free survivorship had a strong relation to better QOL scores ($P < .001$). The adjustment for the DEM, CLN, HTH, and PSO domains reduced the magnitude of the survivorship status relation but, in LTS, remained significant until the addition of the PTS variable. A sizable amount of the variance (68%) in this cancer-specific instrument was explained by the covariates.

Impact of Cancer

Consistent with the other outcome measures, disease-free survivorship had a strong relation to better IOC Positive Impact scores ($P < .001$), as indicated by Model I (Table 4). The adjustment for the CLN covariates reduced the magnitude of the survivorship status relation but remained significant ($P < .05$) through Model VI. The covariates explained only 32% of the variance.

Significant differences based on disease status also were identified with the IOC Negative Impact scores.

Table 4. Regression Coefficients for the Relations Between Survivorship Status (Active Disease Versus Disease Free) and Quality of Life (n=761)

	FACT-G			IOC Positive Impact			IOC Negative Impact		
Model Covariates	R^2	STS vs Active *b* (SE)	LTS vs Active *b* (SE)	R^2	STS vs Active *b* (SE)	LTS vs Active *b* (SE)	R^2	STS vs Active *b* (SE)	LTS vs Active *b* (SE)
Model I. SS	.071	13.3 (4.2)*	12.4 (3)*	.021	1.6 (0.2)*	1.2 (0.1)*	.025	−1.0 (0.1)†	−1.3 (0.1)*
Model II. SS+DEM	.160	12.6 (2)*	11.7 (1.7)*	.136	1.6 (0.4)*	1.3 (0.3)*	.113	−1.1 (0.3)†	−1.2 (0.3)*
Model III. SS+DEM+CLN	.200	13.1 (2.9)*	10.1 (2.7)*	.188	1.6 (0.6)†	1.4 (0.5)‡	.210	−1.2 (0.5)‡	−1.0 (0.4)‡
Model IV. SS+DEM+CLN+HTH	.321	10.6 (2.7)*	9.2 (2.5)*	.195	1.6 (0.6)†	1.3 (0.5)‡	.272	−0.9 (0.5)‡	−0.9 (0.4)‡
Model V. SS+DEM+CLN+HTH+PSO	.489	7.9 (2.4)*	8.1 (2.2)*	.315	1.5 (0.5)†	1.1 (0.5)‡	.422	−0.7 (0.4)	−0.9 (0.4)‡
Model IV. SS+DEM+CLN+HTH+PSO+ PTS	.677	3.7 (1.9)‡	2.8 (1.8)	.317	1.5 (0.5)†	1.1 (0.5)‡	.597	−0.0 (0.3)	−0.1 (0.3)

FACT-G indicates Functional Assessment of Cancer Therapy-General; IOC, Impact of Cancer; R^2, proportion of variation in the dependent variable explained by the regression equation; STS, short-term disease-free survivor (<5 years); Active, patients who self-reported current non-Hodgkin lymphoma; *b*, unstandardized regression coefficient (slope); SE, standard error; LTS, long-term disease-free survivor (≥5 years); SS, survivorship status; DEM, demographic covariates (sex, race, ethnicity, age, income, education, marital status, employment status); CLN, clinical covariates (histology, stage, surgery, radiation therapy, chemotherapy, bone marrow/stem cell transplantation, biologic therapy, recurrence, number of oncology-related visits, site of treatment); HTH, general health covariates (other cancer [excluding skin], comorbidity, years since last physical examination); PSO, psychosocial covariates (social support, appraisal of life threat and treatment intensity, employment and insurance issues); PTS, post-traumatic stress.
*$P < .001$.
†$P < .01$.
‡$P < .05$.

Similar to the Positive Impact scale, accounting for the CLN variables reduced the magnitude of the survivorship status relation. However, differences between survivors with active disease and disease-free survivors became nonsignificant with the addition of the PSO variables for STS and with the addition of the PTS variable for LTS. This model accounted for a sizable 60% of the variance.

DISCUSSION

The current study provides 1 of the first examinations of health status and QOL among NHL survivors. Findings included a strong independent relation between active disease and all outcome measures. However, the relation between survivorship status and most outcomes became nonsignificant on adjustment, which indicates that differences in these measures based on active disease are explained essentially by associated differences in some of the covariates. Only 1 outcome measure continued to elucidate differences between those with and without active disease: the IOC Positive Impact scale. One reason for this may be that the IOC is the only QOL-related measure that contains items related to post-traumatic growth; hence, it may be a more sensitive outcome measure for individuals who are disease-free and are more likely to report having benefited from their cancer experience.

Across most outcome measures, there was evidence of moderation in which the inclusion of the PTS covariate produced the largest increases in R^2 except for the SF-36 PCS and the IOC Positive Impact models, in which adding the HTH covariates and the PSO covariates, respectively, produced the largest increases. These data suggest that survivors who indicate PTS are more likely to report negative health status and QOL, because adjusting for this variable in Model VI erased the difference between active disease scores and disease-free scores. Also, there was evidence that HTH covariates (eg, comorbidity) played a pivotal role in explaining physical health status and functioning and a lesser role in overall QOL. Furthermore, the importance of PSO variables (eg, social support) was evident in the context of cancer-related QOL, as indicated by the largest and second largest increase in R^2 in the IOC Positive Impact and FACT-G models, respectively. Although the current study was not designed to determine the mechanisms linking survivorship status and health-related and QOL-related outcomes, it is likely that active disease contributes to worse outcomes through the increase in emotional and physical distress that is associated with the disease and treatment-related effects.

Unexpectedly, no significant differences were observed between STS and LTS on any of the health or

QOL measures, suggesting that simply time out from diagnosis and treatment is not an explanation for such status after cancer and that PSO effects resolve by or continue beyond the conventional 5-year threshold. Given this finding, survivorship researchers might consider expanding their LTS population to include STS as a means to increase sample size and thereby enhance the power of their statistical analyses. For clinicians, this nonsignificant finding implies that screening for health-related and QOL-related issues related to having had cancer should not conclude before the 5-years postdiagnosis milestone for those who evidenced poor QOL earlier. Other critical elements, such as social support or the alleviation of physical symptoms, play a key role in achieving enhanced functioning, regardless of when these elements occur.

Our finding that most of our age-stratified subgroups scored lower on the MCS than the norms (ie, met criteria for minimally important difference)[33] contrasts with previous studies in which long-term survivors' psychological health approximated that of healthy comparison groups.[2,4,34] The tentative health status of lymphoma patients and the knowledge that their cancer could come back at any time may contribute to a more tenuous or labile emotional health state. However, a difference of 4.1 points on the MCS was <50% of the SD (11.2) in our sample; therefore, the clinical relevance was small. Future studies are needed to examine the clinical meaning of the lower MCS scores, especially in a young survivor cohort.

The relation between having active disease and self-reported health status and QOL has important implications. For example, healthcare professionals may want to give closer attention to survivors who have chronic (active) disease and screen for QOL-related problems. In addition, PSO intervention design and development should consider balancing treatment and control groups based on disease status. For example, individuals with active disease may be more likely to report worse QOL at baseline and may respond differently to specific treatment components than those who are disease-free. Finally, components of PSO (less social support, negative appraisals, and more cancer-related insurance and employment-related issues) and PTS were related to health status and QOL and potentially are modifiable.

There are several limitations in this study. We cannot establish a cause-effect relation between survivorship status and health and QOL status, which is typical for any cross-sectional study. For example, we cannot ensure that the risk factor (active disease) preceded the variables of interest (health status, QOL) because of our inability to assess this cohort over time, which would be possible in a longitudinal design. Furthermore, our sequential models adjusted for many (although likely not all) of the characteristics that may have confounded the relation between survivorship status and outcomes. In addition, the inclusion of patients from only 2 large comprehensive cancer centers in North Carolina may limit the generalizability of our results to survivors who live in other regions and who are treated at smaller hospitals. However, our demographic profile closely mirrors that of the national population of NHL survivors,[35] thereby strengthening the robustness and generalizability of our analyses. Also, the IOC initially was developed for and only tested with off-treatment survivors who are 5 years to 10 years postdiagnosis and appropriately may not be sensitive for those in active treatment, although there are no data to support this possibility. Also, without a matched comparison group based on sociodemographic and comorbid conditions, it is difficult to determine whether these survivors had better or worse status than a similar group of individuals who never had cancer. However, the results of comparisons with general population norms support the need to address health status and functioning concerns in this population, as evidenced by lower PCS scores (for those with active disease) and MCS scores in our sample. Finally, the lower percentage of those with active disease (14%) implies less precise group mean score estimates compared with disease-free survivors.

In summary, the use of general health status and cancer-specific measures revealed significant differences between NHL survivors who reported having active disease and those who were disease-free. In addition, there were no significant differences in outcomes between STS and LTS, which challenges the current use of the 5-year mark in LTS research. These data also illustrate the value of using multiple instruments to assess areas that are particularly relevant to cancer survivors and of studying subgroups with differing disease status.

Conflict of Interest Disclosures

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