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ORIGINAL REPORT

Post-Traumatic Stress Symptoms in Long-Term Non-Hodgkin's Lymphoma Survivors: Does Time Heal?

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ABSTRACT

Purpose
Little is known about the trajectory of post-traumatic stress disorder (PTSD) symptoms in cancer survivors, despite the fact that such knowledge can guide treatment. Therefore, this study examined changes in PTSD symptoms among long-term survivors of non-Hodgkin's lymphoma (NHL) and identified demographic, clinical, and psychosocial predictors and correlates of PTSD symptomatology.

Patients and Methods
Surveys were mailed to 682 NHL survivors who participated in an earlier survey and now were at least 7 years postdiagnosis. Information was obtained regarding PTSD symptoms, positive and negative perceptions of the cancer experience (ie, impact of cancer), and other potential correlates of PTSD.

Results
A total of 566 individuals participated (83% response rate) with a median of 12.9 years since diagnosis; respondents were 52% female and 87% white. Although half (51%) of the respondents reported no PTSD symptoms and 12% reported a resolution of symptoms, more than one-third (37%) reported persistence or worsening of symptoms over 5 years. Survivors who reported a low income, stage ≥ 2 at diagnosis, aggressive lymphoma, having received chemotherapy, and greater impact of cancer (both positive and negative) at the initial survey had more PTSD symptoms at follow-up. In multivariable analysis, income and negative impacts of cancer were independent predictors of PTSD symptoms.

Conclusion
More than one-third of long-term NHL survivors experience persisting or worsening PTSD symptoms. Providers should be aware of enduring risk; early identification of those at prolonged risk with standardized measures and treatments that target perceptions of the cancer experience might improve long-term outcomes.

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INTRODUCTION

Recent advances in treating non-Hodgkin's lymphoma (NHL), one of the most common forms of cancer, have led to a more than doubling of the 5-year relative survival rate from the 1960s, from 31% to 69%.[1] Thus, NHL is often perceived by survivors as a life-long chronic illness, with alternating symptom-free and symptom-exacerbation phases that may require treatment. As with other chronic illnesses, comorbidities are common in the context of NHL, including symptoms of post-traumatic stress disorder (PTSD), which were identified among 39% of NHL survivors[2] and have been shown to be associated with poor quality of life[3-5] and depression[6] in other cancer samples.

PTSD symptoms of avoidance, arousal, and re-experiencing have been identified in individuals diagnosed with an adult cancer in several cross-sectional studies.[2,7,8] A few longitudinal studies have examined cancer-related PTSD during the first year after a diagnosis.[9-11] However, none have examined the trajectory of cancer-related PTSD symptoms in long-term survivors, so nothing is known regarding symptom stability in this population. Furthermore, little is known about the predictors of PTSD in this understudied group of NHL survivors, the knowledge of which may be helpful in identifying those at future need.

Our initial study defined the NHL survivor experience in terms of PTSD,[2] quality of life,[12] and the impact of cancer (IOC).[13,14] That study was cross sectional with a median of 8 years postdiagnosis.

This follow-up assessment resurveyed study participants 5 years later and extends our examination to a median of 13 years postdiagnosis, providing a unique window into the longitudinal NHL experience. The purpose of this follow-up study is to examine change in PTSD symptoms over a 5-year period among NHL survivors and identify demographic, clinical, and psychosocial factors associated with changes in PTSD symptoms. We hypothesized that PTSD symptoms would persist or worsen for a small proportion of the sample, particularly given the potential for disease relapse, and that nonwhite race, younger age, less education and social support, comorbidities, and negative perceptions of the cancer experience would be associated with follow-up PTSD symptoms after controlling for initial PTSD symptoms. These findings have important implications for clinical care and future research on the late effects of NHL diagnosis and treatment.

PATIENTS AND METHODS

Study Design and Patient Recruitment

We conducted a longitudinal follow-up assessment of NHL survivors who consented to an earlier study and were treated at Duke University or the University of North Carolina Cancer Centers. The institutional review boards at both institutions approved this study. Initial study eligibility criteria required that individuals had been diagnosed with NHL $\geq$ 2 years previously and were $\geq$ 19 years of age; details of initial study procedures are published elsewhere.[2] Hence, the study cohort for this study was $\geq$ 7 years postdiagnosis and $\geq$ 24 years of age. The consent form used in the initial study included a statement of willingness to be recontacted within the next 5 years. Follow-up data were collected in 2010; surveys from 2005 and 2010 were linked at the individual patient level to facilitate within-person analyses of change over time.

Procedures

In accordance with the Dillman method for administering surveys,[15] a brief prenotice letter was mailed to patients who were assumed living and within 5 years of their initial study enrollment. The follow-up survey was mailed 2 weeks later and included a postage-paid return envelope, a $2 incentive, and a form to indicate interest in participating in future studies and/or receiving an educational CD and summary of research findings. Thank-you and/or reminder postcards were mailed 2 weeks later, and nonresponders were sent replacement surveys and later telephoned to confirm receipt of the survey.

Instruments

Data collected in this second survey included demographic and clinical status (eg, change in marital status, recurrence of NHL). The Self-Administered Comorbidity Questionnaire (SCQ), a 12-item self-report version of the Charlson Index, was used to assess non–cancer-related problems.[16] In scoring the SCQ, an individual can receive up to 3 points for each of 15 medical conditions (1 point each for presence of the problem, current treatment, and functional limitation; range, 0 to 45 points).

Psychosocial well-being was assessed with the Medical Outcomes Study Social Support Survey (MOS-SSS)[17] and the Impact of Cancer Version 2 (IOCv2) surveys.[13] Scores for the 20-item MOS-SSS range from 20 to 100, with higher scores representing better social support. The IOCv2 assessed the positive life changes and negative impacts attributed to the cancer experience. It includes 37 items to measure four positive (Altruism/Empathy, Health Awareness, Meaning of Cancer, Positive Self-Evaluation) and four negative (Appearance Concerns, Body Change Concerns, Life Interference, Worry) subscales, which total to Positive and Negative Impact Summary scores (range, 1 to 5). Higher Positive Impact Summary scores indicate greater positive perceptions, and higher Negative Impact Summary scores indicate more negative perceptions.

Post-traumatic stress symptoms were measured with the PTSD Checklist-Civilian Version (PCL-C),[18] a self-report symptom checklist that closely mirrors the diagnosis criteria in Diagnostic and Statistical Manual of Mental Disorders, Revision IV (DSM-IV).[19] The instructions were modified so that symptoms were keyed to the particular traumatic stressor of interest; specifically, participants were asked to rate each PTSD symptom in the past 4 weeks with respect to their NHL diagnosis and treatment. Each of 17 symptoms is rated with respect to intensity on a scale of 1 (not at all) to 5 (extremely bothersome). Two approaches were used to construct an aggregate score in assessing symptoms: the continuous score (range, 17 to 85) and the symptom cluster method, which follows the DSM-IV PTSD symptom structure. For example, individuals would be considered as having a PTSD symptom if they reported having been at least moderately bothered by (score $\geq$ 3) at least one of five re-experiencing symptoms (eg, nightmares), at least three of seven avoidance symptoms (eg, evading follow-ups), or at least two of five arousal symptoms (eg, easily startled).

Statistical Analyses

To compare follow-up study participants and nonparticipants with respect to initial demographic, clinical, and psychosocial characteristics and PTSD, we tested for differences between participants and both decedents and nonresponders by using t tests for continuous measures and χ^2 tests for categorical measures. Because initial PTSD symptomatology is one of the strongest predictors of PTSD symptoms at follow-up, all analyses that examined characteristics associated with follow-up PCL-C scores were adjusted for the initial score of this measure. To assess the association between each of the independent variables (ie, data from the initial survey as predictors and from the follow-up survey as correlates) and the follow-up PCL-C, we used a series of linear regression models with

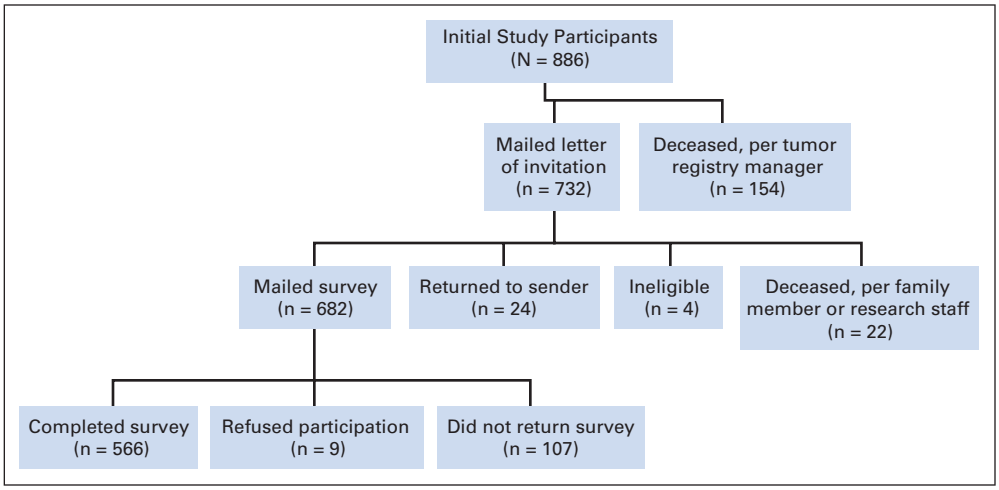

Fig 1. CONSORT diagram.

follow-up PCL-C as the dependent variable. We first tested each independent variable separately (ie, only the candidate variable and initial PCL-C score in the model). Then, variables that were at least marginally significantly associated with follow-up PCL-C in these models ($P < .10$) were included in a multiple linear regression to estimate the independent associations of initial survey predictors with follow-up PCL-C. An additional model was estimated that included both the initial survey predictors and follow-up correlates. For the psychosocial measures, change scores (follow-up score minus initial score) were used rather than follow-up scores, so that the effect of changes in these measures independent of initial status could be evaluated. Data management and statistical analyses were conducted by using SAS Version 9.2 (SAS Institute, Cary, NC).

RESULTS

Patients and Recruitment

Of the 886 initial study participants, 176 had died, four were ineligible (because of change in diagnosis or dementia), and 24 of the mailed surveys were returned as undeliverable at follow-up. Of the 682 eligible individuals who were assumed to have received a follow-up survey, 566 (83%) completed and returned their survey, 107 (16%) did not respond, and nine (1%) refused to participate (Fig 1).

Table 1. Demographic, Clinical, Psychosocial, and Post-Traumatic Stress Characteristics at the Time of the Initial Survey, by Participant Status in the Follow-Up Survey

Characteristic	Participants (n = 566)			Nonparticipants (n = 144)[a]			P[b]
	No.	%	Mean ± SD	No.	%	Mean ± SD	
Demographics							
Female sex	294	51.9		78	54.2		.633
White race	494	87.3		108	75.0		< .001
Income < $30,000	113	22.2		53	41.4		< .001
College or postgraduate degree	242	43.6		50	35.7		.091
Married or living with a partner	452	80.4		96	68.1		.001
Age, years			62.4 ± 12.4			56.7 ± 15.6	< .001
Clinical characteristics							
Had an indolent type of lymphoma	270	50.3		76	55.9		.243
Was diagnosed at stage > I	339	68.1		72	62.3		.224
Had received chemotherapy	446	78.8		103	71.5		.063
Had undergone a transplantation[c]	87	15.4		15	10.4		.130
Had received biologic therapy	166	29.3		30	20.8		.042
Was currently receiving treatment	58	10.4		22	15.6		.083
Had active disease[d]	47	9.1		20	15.9		.027
Had a recurrence of disease	184	33.2		39	28.7		.317
Time since diagnosis, years			10.4 ± 7.1			9.5 ± 6.5	.156
Mean comorbidity score[e]			5.2 ± 4.5			5.8 ± 5.5	.166
Had a second primary cancer	71	12.7		16	11.4		.673
Psychosocial characteristics							
Social Support[f]			83.4 ± 16.0			80.7 ± 17.1	.079
IOC Negative Impact[g]			2.2 ± 0.7			2.3 ± 0.9	.080
IOC Positive Impact[h]			3.5 ± 0.8			3.5 ± 0.8	.978
Post-traumatic stress							
PCL-C total score[i]			26.1 ± 9.0			28.8 ± 11.8	.013
Re-experiencing			6.6 ± 2.6			7.6 ± 4.0	.006
Avoidance/numbing			10.4 ± 4.1			11.4 ± 4.8	.031
Arousal			9.1 ± 3.6			9.8 ± 4.5	.075
PCL-C total score ≥ 44[j]	28	5.0		16	11.6		.004
PCL-C symptoms[k]							
None symptoms	351	62.8		81	58.7		.163
One	132	23.6		28	20.3		
Two	43	7.7		15	10.9		
Three	33	5.9		14	10.1		

Abbreviations: IOC, Impact of Cancer Version 2 (IOCv2) [survey]; PCL-C, Post-Traumatic Stress Disorder (PTSD) Checklist, Civilian Version.
[a]Assumed living; of the 886 initial survey participants, 176 were confirmed to be deceased at follow-up.
[b]P value for comparison of participants and nonparticipants based on χ^2 for percentages and t test for means.
[c]Bone marrow or stem-cell transplantation.
[d]Was not in remission or cured of non-Hodgkin's lymphoma.
[e]Self-Administered Comorbidity Questionnaire score; possible range, 0-42.
[f]Medical Outcomes Study Social Support Survey total score; possible range, 0-100; higher scores indicate more support.
[g]Impact of Cancer-Negative Impact Summary score; possible range, 1-5; higher scores indicate greater negative impacts.
[h]Impact of Cancer-Positive Impact Summary score; possible range, 1-5; higher scores indicate greater positive impacts.
[i]PCL-C continuous score; possible range, 17-85; higher scores indicate more symptoms (lower quality of life).
[j]PCL-C continuous score that is equal to or exceeds 44 is indicative of PTSD.[18]
[k]PCL-C symptom score; symptomatology is indicated by score ≥ 3 in one or more re-experiencing items, three or more avoidance items, or two or more arousal items; more symptoms indicate lower quality of life; three symptoms are indicative of PTSD.

Initial demographic, clinical, and psychosocial characteristics and PTSD symptoms of the 566 individuals who participated in the follow-up study and the 144 nonresponders are provided in Table 1. The mean and median time since diagnosis for all participants was 10.4 and 8.0 years, respectively; the median time since diagnosis for the subset that reported a recurrence was 8.8 years. Compared with decedents (not shown in Table 1), follow-up study participants were more likely to report the following characteristics on the initial survey: income $\geq$ \$30,000, college degree, married or living with a partner, younger age, aggressive lymphoma, no current treatment, no active disease, lower comorbidity, lower IOC Negative Impact Summary score, lower PCL-C score, and fewer PTSD symptoms (all $P < .05$). In addition, follow-up study participants compared with nonresponders were more likely to report white race, income $\geq$ \$30,000, married or living with a partner, older age, received biologic therapy, no active disease, and lower PCL-C scores (all $P < .05$). At follow-up, 41 (7.3%) of 557 had a PCL-C score $\geq$ 44, which is indicative of PTSD,[20] whereas 28 (5.0%) of 557 scored $\geq$ 44 at the time of the initial survey. The most common PCL-C problems endorsed by participants as moderately to extremely bothersome were sleep and concentration difficulties and loss of interest in activities (Table 2).

PTSD Symptoms Over Time in Long-Term NHL Survivors

The follow-up survey was completed an average of 4.8 years after initial survey completion (range, 4.3 to 5.4 years). Total and subscale scores for the comparison of the initial survey and the follow-up PCL-C are listed in Table 3. Paired *t* tests found no significant change in mean scores reported by the 557 participants who completed the PCL-C at initial and follow-up surveys. However, the avoidance/numbing subscale had the largest mean change or increase in symptoms of 0.2 (standard deviation, 3.6; $P = .15$).

Table 4 provides a cross tabulation of PTSD symptoms at the time of the initial survey and follow-up. Among the 557 participants who completed the PCL-C at both times, 281 (50.4%) did not report symptoms at either time point, 68 (12.2%) reported a resolution of symptoms, 23 (4.1%) reported improvement but persistent symptoms, 79 (14.2%) reported stable and persistent symptoms, and 106 (19.0%) reported a worsening of symptoms. In addition, 73 (13.1%) reported a 5- to less than 10-point increase in PCL-C scores, which represents reliable change (ie, worsening not due to chance). In addition, 39 (7.0%) reported at least a 10-point increase, considered to be a clinically significant worsening of symptoms. Conversely, 88 (15.8%) reported at least a 5-point decrease in PCL-C scores (ie, improvement of symptoms).[21]

Table 2. PCL-C Items Endorsed by Participants As Moderately to Extremely Bothersome at Follow-Up

Item No.	PCL-C Item*	%
13	Trouble falling or staying asleep	38.1
15	Having difficulty concentrating	25.2
9	Loss of interest in activities that you used to enjoy	22.2
12	Feeling as if your future will somehow be cut short	18.3
16	Being "super-alert" or watchful or on guard	18.2
14	Feeling irritable or having angry outbursts	16.4
10	Feeling distant or cut off from other people	15.8
17	Feeling jumpy or easily startled	14.0
8	Trouble remembering important parts of the cancer and its treatment	12.5
1	Repeated, disturbing memories, thoughts, or images of the cancer and its treatment	12.4
6	Avoiding thinking about or talking about the cancer and its treatment or avoiding having feelings related to it	10.6
11	Feeling emotionally numb or being unable to have loving feelings for those close to you	10.5
4	Feeling very upset when something reminded you of the cancer and its treatment	8.0
7	Avoiding activities or situations because they reminded you of the cancer and its treatment	5.5
3	Suddenly acting or feeling as if the cancer and its treatment were happening again (as if you were reliving it)	5.2
2	Repeated, disturbing dreams of the cancer and its treatment	4.8
5	Having physical reactions (for example, heart pounding, trouble breathing, or sweating) when something reminded you of the cancer and its treatment	4.4

Abbreviation: PCL-C, Post-Traumatic Stress Disorder (PTSD) Checklist, Civilian Version.
*PCL-C symptom clusters: at least one re-experiencing item (1-5); at least three avoidance/numbing items (6-12); and at least two arousal items (13-17).

Predictors and Correlates of PTSD Symptoms in Long-Term NHL Survivors

The results of linear regression models are provided in Table 5, the first set of models adjusting only for initial PCL-C score, the second model adjusting for initial PCL-C score and significant predictors (initial survey responses), and the third model adjusting for initial PCL-C score, significant predictors, and significant correlates (follow-up survey responses). For the models with adjustment for initial PCL-C only (Column 1), the initial survey predictors of having PTSD symptoms at follow-up were income less than \$30,000 ($P < .001$), having an aggressive lymphoma ($P = .025$), stage $\geq$ II at diagnosis ($P = .007$), having had chemotherapy ($P = .027$), and IOC Negative Impact Summary ($P < .001$) and IOC Positive Impact Summary ($P = .006$) scores. A recurrence in the last 5 years ($P = .011$), higher follow-up comorbidity score ($P = .003$), and increase in IOC Negative Impact Summary score ($P < .001$) were associated with higher follow-up PCL-C. For the multiple linear regression model with adjustment for initial PCL-C and other initial survey measures (Column 2), the significant independent predictors of having more PTSD symptoms at follow-up were income less than \$30,000 ($P < .001$) and IOC Negative Impact Summary score ($P < .001$). Regarding the multiple linear regression model with adjustment for initial PCL-C, other initial measures, and changes in status between the initial survey and follow-up (Column 3), the significant initial survey predictors of greater PTSD symptoms at follow-up were income less than \$30,000 ($P < .001$), not currently receiving treatment ($P = .013$), and IOC Negative Impact Summary ($P < .001$) and IOC Positive Impact Summary ($P = .030$) scores. Increase in IOC Negative Impact Summary score was also a significant correlate of follow-up PCL-C ($P < .001$). For the models in Columns 2 and 3, R^2 values were 0.55 and 0.65, respectively, indicating that the demographic, clinical, and psychosocial variables accounted for a substantial amount of the variance in follow-up PCL-C.

To shed further light on the findings related to negative and positive impacts, Table 6 provides the IOC Subscale predictors and correlates of follow-up PCL-C, with three models again controlling for initial PCL-C and other factors. For the linear regression model with adjustment for initial PCL-C only (Column 1), all of the IOC Negative

Table 3. Comparison of Initial and Follow-Up PCL-C Scores (n = 557)*

Outcome	Initial Survey		Follow-Up Survey		Change (Δ) Between Initial and Follow-Up Surveys		95% CI for Mean [δ]	*t*	*P*
	Mean	SD	Mean	SD	Mean	SD			
PCL-C total score	26.1	9.0	26.4	9.6	0.3	7.4	−0.4 to 0.9	0.79	.43
Re-experiencing	6.6	2.6	6.5	2.7	−0.1	2.5	−0.3 to 0.1	−0.72	.47
Avoidance/numbing	10.4	4.1	10.6	4.3	0.2	3.6	−0.1 to 0.5	1.44	.15
Arousal	9.1	3.6	9.2	3.9	0.1	3.2	−0.1 to 0.4	0.77	.44

Abbreviations: PCL-C, Post-Traumatic Stress Disorder (PTSD) Checklist, Civilian Version; SD, standard deviation.
*PCL-C continuous score; total score possible range, 17-85; re-experiencing score possible range, 5-25; avoidance/numbing score possible range, 7-35; arousal score possible range, 5-25; higher scores indicate more symptoms (lower quality of life).

and Positive Impact Subscale scores were significant predictors of more PTSD symptoms at follow-up (all $P < .05$), except "Health Awareness." In addition, increases in IOC Negative Impact Subscale scores were associated with greater PTSD symptoms at follow-up (all $P < .001$), but there were no associations for change in Positive Impact Subscale scores. For the model with adjustment for initial PCL-C and other initial measures (Column 2), a higher "Worry" score was the only IOC Subscale associated with more PTSD symptoms at follow-up ($P = .019$). Regarding the multiple linear regression model adjusted for initial PCL-C and other initial and follow-up measures (Column 3), IOC Negative Impact "Appearance Concerns," "Life Interferences," and "Worry" scores were significant initial survey predictors of more follow-up PTSD symptoms (all $P < .05$). Further, increases in IOC Negative Impact "Life Interferences" and "Worry" scores were independently associated with higher PCL-C scores (both $P < .001$). In addition, a decrease in the IOC Positive Impact "Positive Self-Evaluation" score was an independent correlate of follow-up PCL-C ($P = .005$).

DISCUSSION

In this follow-up study, the largest longitudinal study of PTSD symptomatology among adult cancer survivors reported in the literature to date, we found that although 51% of survivors did not have PTSD symptoms at either time point, and 12% had PTSD symptoms that resolved over 5 years, more than one third of the sample reported persistent (18%) or worsening (19%) PTSD symptoms over a 5-year period. These findings of persistent PTSD symptomatology among NHL survivors are consistent with those found among disaster victims[22,23] and victims of violence.[24-26] Importantly, several characteristics were identified that could help screen and target treatments for those survivors who are at risk for prolonged PTSD symptoms and inform opportunities to reduce the impact of potentially PTSD-inducing cancer care scenarios.

Although our hypotheses were partially supported (eg, finding of persisting and worsening of symptoms), we found that the explanation for follow-up PTSD symptoms was not limited to recurrence status. Specifically, individuals with an initial status of lower income, aggressive lymphoma, stage ≥ II at diagnosis, having had chemotherapy, and higher IOC Negative and Positive Impact Summary scores were more likely to have more PTSD symptoms 5 years later. Importantly, income and Negative Impacts were most influential in adjusted analyses (ie, more strongly predictive of PTSD symptoms) than the clinical aspects of the disease and treatment.

How might these findings be used? Two strong messages emerge: (1) the upfront cancer treatment experience directly influences downstream patient experience and risk of PTSD, and (2) specific individuals are at increased risk. Therefore, whole-person interventions

Table 4. Cross Tabulation of PCL-C Symptom Scores at Initial and Follow-Up Surveys (n = 557)

Post-Traumatic Stress Symptoms at Initial Survey*	Post-Traumatic Stress Symptoms at Follow-Up Survey									
	0		1		2		3		Total	
	No. of Patients	%	No. of Patients	%	No. of Patients	%	No. of Patients	%	No. of Patients	%
0	281	80.3	51¶	14.6¶	11¶	3.1¶	7¶	2.0¶	350	62.8
1	53†	40.2†	46§	34.8§	20¶	15.2¶	13¶	9.8¶	132	23.7
2	12†	28.6†	11‡	26.2‡	15§	35.7§	4¶	9.5¶	42	7.5
3	3†	9.1†	9‡	27.3‡	3‡	9.1‡	18§	54.5§	33	5.9
Total	349	62.7	117	21.0	49	8.8	42	7.5	557	100

Abbreviation: PCL-C, Post-Traumatic Stress Disorder (PTSD) Checklist, Civilian Version.
*PTSD symptoms are re-experiencing, avoidance/numbing, and arousal; higher scores represent more symptoms (ie, lower quality of life); three symptoms are indicative of PTSD.
†Resolved or no symptoms.
‡Improved but persistent symptoms.
§Stable and persistent symptoms.
¶Worsening symptoms.

Table 5. Predictors and Correlates of Post-Traumatic Stress: PCL-C[a]

Characteristic	Column 1 Adjusted for Initial PCL-C[b]			Column 2 Adjusted for Initial PCL-C and Other Predictors (n = 521)[c]			Column 3 Adjusted for Initial PCL-C, Other Predictors, and Correlates (n = 519)		
	Coefficient β	SE	*P*	Coefficient β	SE	*P*	Coefficient β	SE	*P*
Initial PCL-C[d]	0.73	0.03	< .001	0.60	0.05	< .001	0.51	0.04	< .001
Initial survey demographic variables									
Female sex	−0.82	0.60	.169						
White race	1.31	0.91	.145						
Income < $30,000	3.34	0.73	< .001	3.84	0.77	< .001	3.06	0.67	< .001
Less than college degree	0.28	0.61	.649						
Not married	0.27	0.76	.718						
Age at study enrollment	−0.01	0.02	.556						
Initial survey clinical variables									
Had an indolent type of lymphoma	−1.38	0.61	.025	−0.75	0.65	.249	−0.22	0.58	.707
Stage I at diagnosis	−1.80	0.66	.007	−1.00	0.71	.163	−0.48	0.63	.443
Had received chemotherapy	1.62	0.73	.027	0.50	0.81	.540	0.33	0.71	.647
Had undergone a transplantation[e]	1.24	0.83	.136						
Had received biologic treatment	−0.42	0.66	.520						
Was currently receiving treatment	−1.91	0.97	.050	−1.88	1.00	.059	−2.20	0.88	.013
Had active disease[f]	0.99	1.08	.357						
Recurrence status[g]									
Had one or more recurrences	−0.21	0.65	.740						
Was never in remission	−1.59	1.38	.250						
Years since diagnosis	0.03	0.04	.456						
Comorbidity score[h]	0.07	0.07	.299						
Had a second primary cancer	−0.57	0.90	.523						
Initial survey psychosocial variables									
Social Support[i]	0.01	0.02	.987						
IOC Negative Impact[j]	2.55	0.60	< .001	2.71	0.61	< .001	4.51	0.58	< .001
IOC Positive Impact[k]	1.06	0.38	.006	0.42	0.40	.296	0.77	0.35	.030
Follow-up clinical correlates									
Was currently receiving treatment	1.47	1.15	.202						
Had active disease	−1.66	1.07	.121						
Recurrence status									
Had a recurrence in last 5 years	1.92	0.76	.011				0.72	0.68	.294
Was never in remission	0.46	1.33	.732						
Comorbidity score	0.33	0.11	.003				0.09	0.10	.389
Had treatment in last 5 years	−1.04	0.68	.127						
Had a new cancer in last 5 years	0.72	1.06	.496						
Follow-up psychosocial correlates									
Social Support	−0.03	0.02	.120						
Δ IOC Negative Impact	5.18	0.50	< .001				6.05	0.51	< .001
Δ IOC Positive Impact	−0.09	0.51	.857						
Model-adjusted R^2[l]		0.47			0.55			0.65	

Abbreviations: IOC, Impact of Cancer Version 2 (IOCv2) [survey]; PCL-C, Post-Traumatic Stress Disorder (PTSD) Checklist, Civilian Version.
[a]PCL-C continuous score; total score possible range, 17-85.
[b]Baseline PCL-C; number of patients ranges from 493 to 557.
[c]Regression models also adjusted for missing data (ie, income and stage dummy variables).
[d]Baseline PCL-C; R^2 ranges from 0.46 to 0.56.
[e]Bone marrow or stem-cell transplantation.
[f]Was not in remission or cured of non-Hodgkin's lymphoma.
[g]No recurrence *v* had at least one recurrence, never in remission.
[h]Self-Administered Comorbidity Questionnaire score; possible range, 0-42.
[i]Medical Outcomes Study Social Support Survey total score; possible range, 0-100; higher scores indicate more support.
[j]IOC-Negative Impact Summary score; possible range, 1-5; higher scores indicate greater negative impacts.
[k]IOC-Positive Impact Summary score; possible range, 1-5; higher scores indicate greater positive impacts.
[l]Column 1 represents initial PCL-C score R^2 statistic.

targeted at improving the experience of patients with NHL, including mitigating PTSD, could seek to do either or both of the following: (1) improve those elements of the treatment experience that lead to negative impressions (eg, reducing life interference by social work intervention, improving a sense of body image by physical therapy, relieving worry by cognitive behavioral therapy), and (2) recognize that NHL survivors from poor socioeconomic circumstances are at the highest risk and triage efficiently to social support services. In addition, clinical care should include a formal assessment of symptoms that includes domains similar to those on the IOC. However,

Table 6. IOC Subscale As a Predictor and Correlate of Post-Traumatic Stress: PCL-C*

Subscale Item	Column 1 Adjusted for Initial PCL-C†			Column 2 Adjusted for Initial PCL-C and Other Predictors (n = 512)‡			Column 3 Adjusted for Initial PCL-C, Other Predictors, and Correlates (n = 508)§		
	Coefficient, β	SE	*P*	Coefficient, β	SE	*P*	Coefficient, β	SE	*P*
IOC predictors									
Negative Impact¶									
Appearance Concerns	1.07	0.40	.008	0.77	0.42	.071	1.15	0.44	.010
Body Change	1.17	0.31	< .001	0.53	0.36	.142	0.24	0.40	.544
Life Interferences	1.98	0.58	< .001	0.44	0.70	.529	1.61	0.72	.027
Worry	0.85	0.38	.024	0.98	0.42	.019	1.88	0.41	< .001
Positive impact‖									
Altruism/Empathy	0.80	0.32	.012	0.25	0.44	.565	0.30	0.39	.432
Health Awareness	0.47	0.36	.193						
Meaning of Cancer	0.67	0.28	.016	0.46	0.35	.191	0.53	0.31	.089
Positive Self-Evaluation	0.69	0.30	.023	−0.36	0.45	.421	−0.30	0.44	.498
IOC correlates									
Change (Δ) in Negative Impact									
Δ Appearance Concerns	1.57	0.37	< .001				0.60	0.44	.173
Δ Body Change	1.93	0.32	< .001				0.79	0.41	.052
Δ Life Interferences	3.62	0.43	< .001				2.80	0.55	< .001
Δ Worry	2.97	0.36	< .001				2.02	0.44	< .001
Δ Positive Impact									
Δ Altruism/Empathy	0.51	0.39	.195						
Δ Health Awareness	0.44	0.34	.193						
Δ Meaning of Cancer	−0.30	0.33	.365						
Δ Positive Self-Evaluation	−0.70	0.36	.053				−1.00	0.34	.005

Abbreviations: IOC, Impact of Cancer Version 2 (IOCv2) [survey]; PCL-C, Post-Traumatic Stress Disorder (PTSD) Checklist, Civilian Version.
*PCL-C continuous score; total score possible range, 17-85.
†No. of patients ranges from 493 to 557.
‡Regression model adjusted for initial PCL-C demographic, clinical, and psychosocial predictors and missing data (ie, income and stage dummy variables).
§Regression model adjusted for initial PCL-C demographic, clinical, and psychosocial predictors; follow-up clinical and psychosocial correlates; and missing data (ie, income and stage dummy variables).
¶IOC-Negative Impact Summary score; possible range, 1-5; higher scores indicate greater negative impacts.
‖IOC-Positive Impact Summary score; possible range, 1-5; higher scores indicate greater positive impacts.

additional testing of the IOC in other samples is needed to support its use earlier in the cancer trajectory.

Although there are no known psychosocial interventions developed specifically for NHL survivors, evidence-based offerings could be tailored to meet the unique needs of this population. The alternating symptom-free and symptom exacerbation characteristics of NHL coupled with the difficulty in distinguishing between signs of aging and long-term symptoms from treatment may exacerbate worry or fear of recurrence in survivors. The Managing Uncertainty Day-to-Day intervention[27] is designed to help older breast cancer survivors manage fears of recurrence and improve coping skills by delivering cognitive strategies via audiotape. In addition, a supportive-expressive group therapy intervention has been shown to significantly reduce trauma symptoms and mood disturbance in women with advanced breast cancer.[28] Thus, treatments exist that might benefit PTSD outcomes of NHL survivors, especially if they are targeted to those of greatest presumed risk.

The findings in this study are especially beneficial, given the large sample size, excellent response rate, use of standardized measures, and longitudinal design. Although our study included only two survey administrations, it is a starting point of depicting the experiences of patients with cancer. Study limitations include the representation of a predominantly married and white sample and potential nonresponse bias. However, our racial profile closely mirrors that of the national population of NHL survivors, thereby strengthening the generalizability of our findings. There is also evidence that individuals who chose not to participate at follow-up were not doing well at the initial survey; therefore, the level of PTSD symptomatology may be underestimated. Second, the 28-page survey lacked measures assessing other psychological problems and life stressors in an effort to minimize the burden on respondents. Third, potential biases inherent in the use of self-report measures were minimized by using standardized instruments. And last, there is a potential overlap of PTSD symptoms with those related to cancer and treatment. However, only a small proportion (9.4%) of the sample reported active NHL or receiving treatment at follow-up. Furthermore, follow-up disease and treatment status were not predictive of PTSD symptoms in the linear regression analysis.

In conclusion, this article provides new information about the trajectory of PTSD symptoms in long-term NHL survivors. The initial cancer experience (and the need to improve it) becomes paramount in improving downstream outcomes, such as PTSD symptomatology. In addition, the identification of several patient characteristics related to PTSD risk could inform the screening process early in the survivorship trajectory. Furthermore, the strong predictive role of the IOC is consistent with previous cross-sectional studies and suggests that negative perceptions related to the cancer experience could be targeted in

interventions as a means to minimize PTSD symptomatology. Future work should focus on the identification of patients at risk by using predictive models applied at the point of care and development of low-cost interventions that are delivered to those exhibiting clinically significant PTSD symptomatology during treatment to improve the long-term patient experience.

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Data analysis and interpretation: All authors
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