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ORIGINAL ARTICLE

Work and education interruption in long-term Hodgkin lymphoma survivors: an analysis among patients from nine EORTC-LYSA trials

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ABSTRACT

Background: Disease-specific studies on the impact of Hodgkin lymphoma (HL) on education or work interruption and resumption are lacking.

Material and methods: In a cross-sectional study conducted among long-term HL survivors enrolled from 1964 to 2004 in nine randomised EORTC-LYSA trials, the interruption and resumption of education/work was investigated. Survivors alive 5–44 years after diagnosis who were studying or working at time of diagnosis were included ($n = 1646$). Patient and treatment characteristics were obtained from trial records. Education and work outcomes were collected using the Life Situation Questionnaire. Logistic regression was used to model education or work interruption; Cox regression was used to study resumption rates.

Results: Among survivors studying at time of diagnosis ($n = 323$), 52% (95% CI: 46–57%) interrupted their education; however, it was resumed within 24 months by 92% (95% CI: 87–96%). The probability of interruption decreased with time: the more recent the treatment era, the lower the risk (OR 0.70 per 10 years, 95% CI: 0.49–1.01). Treatment with radiotherapy (yes vs. no) was associated with a higher education resumption rate (HR 2.01, 95% CI 1.07–3.78) whereas age, sex, stage, radiotherapy field and chemotherapy were not.

Results: Among survivors working at time of diagnosis ($n = 1323$), 77% (95% CI: 75–79%) interrupted their work. However, it was resumed within 24 months by 86% (95% CI: 84%-88%). Women were more likely to interrupt their work as compared to men (OR 1.90, 95% CI: 1.44–2.51) and, when interrupted, less likely to resume work (HR 0.70, 95% CI: 0.61–0.80). Survivors with a higher educational level were less likely to interrupt their work (OR 0.68 for university vs. no high school, 95% CI: 0.46–1.03); and when interrupted, more likely to resume work (HR 1.50 for university vs. no high school, 95% CI: 1.21–1.86). Increasing age was also associated with lower resumption rates (HR 0.62 for age $\geq$50 vs. 18–29 years, 95% CI: 0.41–0.94).

Conclusion: An interruption in education/work was common among long-term HL survivors. However, most of the survivors who interrupted their studies or work had resumed their activities within 24 months. In this study, no associations between survivors' characteristics and failure to resume education were observed. Female sex, age $\geq$50 years, and a lower level of education were found to be associated with not resuming work after treatment for HL.

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Background

Follow-up studies of successfully treated Hodgkin lymphoma (HL) patients have revealed that cancer treatment comes with a cost – it is associated with a wide range of physical, psychological and socioeconomic problems which may have a long-term impact on the lives of HL survivors [1–4]. While there is an extensive knowledge about late excess morbidity and mortality among HL survivors [5], little is known about the psychosocial consequences caused by the disease including the impact of HL diagnosis and treatment on subsequent career and professional life.

More than 70% of patients diagnosed with HL are in the prime of their educational and employment years [6,7]. Yet, education or work interruption and resumption following HL diagnosis have not previously been studied in a large multicentre setting. Prior studies on education/work among HL survivors often focus on a variety of psycho-medical problems (which bring occupational activities to be examined less thoroughly) or are based on single institution samples [3,8–13]. Commonly, newly diagnosed cancer patients interrupt their work, and most are able to return to work within three years after the interruption [8,14]. However, the characteristics of work interruption, and resumption, are strongly associated with cancer site [14,15]. Since HL often occurs at a young age and the success in treatment has led to an immense increase in the prevalence of HL survivors, knowledge about education and work interruption and resumption of long-term HL survivors seems highly relevant.

In this study, we therefore aimed to investigate the prevalence of education or work interruption and resumption as well as associated factors among HL survivors using the database of the European Organisation for Research and Treatment of Cancer (EORTC) lymphoma group in combination with patient reported outcome measures from the Life situation Questionnaire.

Materials and methods

Study design and patients

A total of 6658 patients from 13 European countries with newly diagnosed, histologically confirmed HL were enrolled in nine consecutive randomised trials (referred to as the H1-H9 trials) between 1964 and 2004 by the EORTC Lymphoma Group and, from 1993, by the Groupe d'Etude des Lymphomes de l'Adulte (GELA now LYSA). Treatment details and results of the individual trials have been published elsewhere [16–25]. Of note, most studies (7 out of 9) were conducted in patients diagnosed with stage I–II disease.

To study a wide spectrum of consequences of HL treatment (including socio-economic and emotional costs), the EORTC Lymphoma Group developed the Life Situation Questionnaire (LSQ). The LSQ is a unique, wide-ranging patient reported outcomes questionnaire, specially developed for HL survivors. It addresses multiple issues such as education and work status (both during treatment and at the time of investigation) not covered in other validated questionnaires [26]. So far fertility, parenthood, long-term fatigue, and cardiovascular disease have been evaluated [27–32]. Between 2009 and 2011, the LSQ was sent by mail (as part of a cross-sectional study) to all HL survivors from the H1–H9 trials known to be alive at last follow-up and with a registered address. Due to privacy laws, patients could not be tracked down directly, this had to be done via their original treating physician [27]. Also, because of the sensitive nature of the questionnaire, only one reminder was sent after 5 weeks [27]. The education and work situation were assessed with several questions such as 'before diagnosis of your Hodgkin's disease, were you employed/working?' and correspondingly 'if you were a student/pupil at the time of first diagnosis, were you able to carry on and finish your education?'. The interruption time was evaluated using the following questions 'after your first diagnosis of Hodgkin's disease, did you stop or interrupt your education/work?' – if yes, 'did you resume your education/work after this stop?' (for further details see Supplementary Annexe 1). Long-term HL survivors who either studied or worked and were $\geq$18 years of age at the time of the first diagnosis were included in the analysis. For the whole cohort, information on baseline patient and treatment demographics were extracted from the EORTC database, including stage of the disease at diagnosis (according to the Ann Arbour classification), treatment exposure and information about (any) relapse. Only data on relapses within 6 months of diagnosis are presented since an early relapse is expected to have the greatest impact on education/work interruption and resumption. Information on education and work interruption and its duration ($<$ or $\geq$1 month) was derived from the LSQ (Supplementary Annexe 1 + 2).

Statistical analysis

Logistic regression was used to model education or work interruption and Cox regression was used to study resumption rates. Subjects who reported they did not resume education or work within five years were considered as censored at five years in all analyses of education and work resumption. Age ($<$18 years vs. $\geq$18 years of age in education analyses and 18–29 vs. 30–39 vs. 40–49 vs. $\geq$50 years of age in work analyses), sex, clinical stage (I vs. II vs. III or IV), radiotherapy use in first line treatment (yes vs. no), chemotherapy use in first-line treatment (yes vs. no), treatment era (year of treatment start modelled as a numerical covariate), educational level (no high school diploma vs. high school diploma vs. university degree; only for work analyses), and country (the Netherlands vs. France vs. Belgium vs. other) were included as covariates in the models. Interaction between radiotherapy and chemotherapy was tested and excluded since it was not statistically significant. For categorical covariates with more than two categories, the inference was based on the global Wald test. To test differences between specific categories Tukey-Kramer post-hoc comparisons were used. To allow for non-linear effects, treatment era was initially modelled using restricted cubic splines with three knots located at the 5th, 50th, and 95th percentiles [33]. Since no evidence of non-linearity was apparent, only the linear term

was retained in the model and estimates of the effect of an increase of 10 years were provided. Because of a small number of missing values (for all populations, the number of complete cases was above 93%), complete case analysis was performed. The Wilson score interval was used for interval estimation of proportions. Resuming education and work across a period of five years was described using the Kaplan-Meier curves. The confidence intervals of the estimates of the proportion of HL survivors who resumed education or work at 3 months, 6 months, 1 year, 2 years, and 5 years after the interruption were based on the log[-log(survival)], with the variance estimate based on the Greenwood formula. The median time until education and work resumption were estimated using the inverse Kaplan-Meier method. The proportionality assumption in the Cox regression models was checked using the approach based on cumulative sums of martingale residuals [34]. In the case of a violation of the assumption, time-varying covariates were introduced to the model using restricted cubic splines with three knots located at the 5th, 50th, and 95th percentiles.

In addition, sensitivity analyses were performed. First, patients treated before 1985 were excluded from the regression analyses of education and work resumption. Second, the regression analyses of education and work resumption stratified by trial were performed.

All tests were carried out at a two-sided significance level of 0.05. Point estimates and two-sided 95% confidence intervals are provided for all estimated parameters.

Results

Among the 6658 HL patients in the EORTC database, 3661 were eligible to receive the LSQ and 2037 (56%) HL survivors responded (see flowchart, Figure 1). The median time between diagnosis and filling in the LSQ was 14.0 years (IQR: 10–19).

Characteristics of the study population are presented in Table 1. Among the LSQ responders studying at the time of diagnosis ($n = 323$), 41.5% were male and the median age was 19.8 (IQR: 17.8–21.5). Most of the responders (18.9 and 67.5%, respectively) were treated for stage I or II disease, while 13.6% were treated for stage III or IV disease. The majority had been treated with radiotherapy (87.9%) and/or chemotherapy (78.3%) and only 2.2% had experienced (any) relapse within 6 months from treatment start. In terms of geographic location, most participants lived in the Netherlands (47.1%) or France (34.7%), followed by Belgium (9.6%). Only a small proportion (11.8%) was treated before 1985 (Table 1). Characteristics of students who had no education interruption compared to those who had are shown in the supplement (Supplementary Annexe 3).

Among the LSQ responders studying at the time of diagnosis, 52% (95% CI: 46–57%) interrupted their education for $\geq$1 month; however, it was resumed within 24 months by 92% (95% CI: 87–96%) with a median education interruption time of 9 months (95% CI: 8–10) (Table 2). The probability of interruption decreased with time: the more recent the treatment era, the lower the risk (OR 0.70 per 10 years, 95% CI 0.49–1.01) (Table 3). Treatment with radiotherapy was associated with a higher education resumption rate (HR 2.01 for 'yes' vs. 'no', 95% CI 1.07–3.78), whereas age, sex, stage, radiotherapy field (data not shown) and chemotherapy were not (Table 3). The effect of country varied over time (non-proportional hazards). Stratification by trial and exclusion of patients treated before 1985 had little impact on the reported estimates (data not shown). For unadjusted estimates see supplement (Supplementary Annexe 5).

Among the LSQ responders working at time of diagnosis ($n = 1323$), 53.9% were male and the majority were 18–40 years old (74.1%). Most of the responders (24.9% and 61.0%, respectively) were treated for stage I or II disease, while 14.0% were treated for stage III or IV disease. The majority had been treated with radiotherapy (87.9%) and/or chemotherapy (81.5%) and only 1.1% had experienced (any) relapse within 6 months from treatment start. Chemotherapy was given for 8–12 weeks (10.5%), 16–18 weeks (33.6%), or for 24 weeks or longer (37.1%). LSQ responders primarily lived in the Netherlands (45.2%), France (39.2%), or Belgium (7.7%), and educational level was equally distributed with approximately one third having no high school diploma (32.1%), a high school diploma (34.9%), and a university degree (31.6%). Only 12.1% were treated before 1985.

Among the LSQ responders working at the time of diagnosis, 77% (95% CI 75–79%) interrupted their work for $\geq$1 month; of those, 86% (95% CI: 84–88%) had resumed work within 24 months with a median work interruption time of 12 months (95% CI: 11–12) (Table 2). The proportion of patients who interrupted work by subgroups is available in the supplement (Supplementary Annexe 4). Women were more likely to interrupt their work as compared to men (OR 1.90, 95% CI 1.44–2.51) and, when interrupted, less likely to resume work (HR 0.70, 95% CI 0.61–0.80) (Table 3). HL survivors with a higher educational level were less likely to interrupt work (OR 0.68 for university vs. no high school, 95% CI 0.46–1.03) and when interrupted, more likely to resume work (HR 1.50 for university vs. no high school, 95% CI 1.21–1.86) (Table 3). Age at treatment $\geq$50 years was also associated with lower resumption rates (HR 0.62 for age $\geq$50 vs. 18–29, 95% CI 0.41–0.94) whereas country, radiotherapy fields (data not shown) and treatment era were not (Table 3). Longer duration of chemotherapy ($\geq$24 vs. 8–12 weeks) also showed lower resumption rates, but only in the first year. No evidence of differences between chemotherapy duration 16 to 18 weeks and 8 to 12 weeks was apparent ($p = 0.90$). Also in this case, a stratification by trial and exclusion of patients treated before 1985 had minor impact on the reported estimates (data not shown). Estimated probabilities by all covariates of resumption of education and work across a period of five years following the interruption are presented in the supplement (Supplementary Annexe 7 + 8).

Discussion

The ability to resume normal activities, such as education/-work, has been shown to be an important indicator of re-adaptation into normal life and of psychosocial recovery after

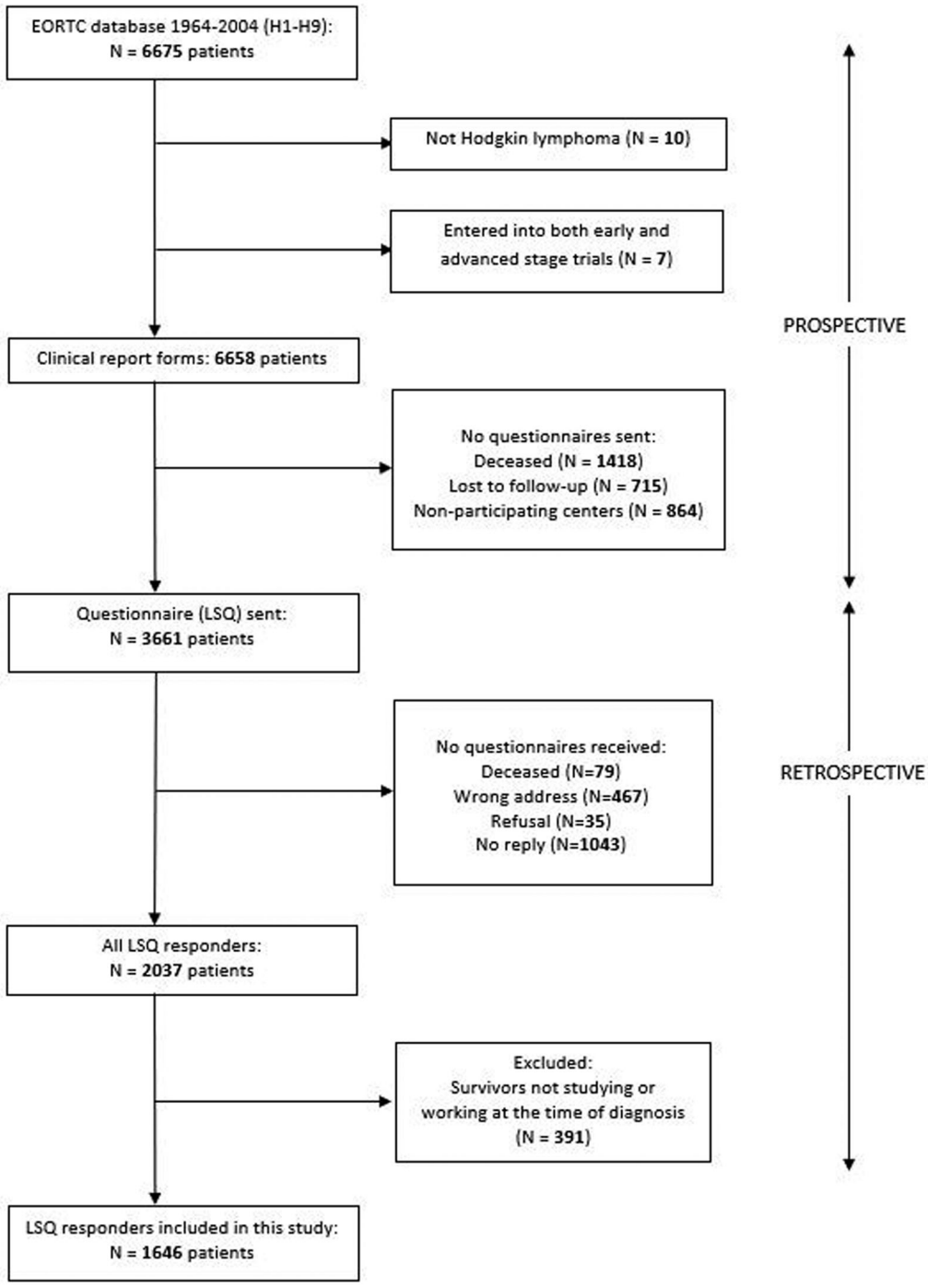

Figure 1. Patient flowchart.

cancer treatment [35]. Furthermore, the ability to return to or maintain educational and occupational pursuits after a cancer diagnosis has been demonstrated to improve quality of life (both from an economic and a social perspective), reduce social isolation and increase self-esteem [8].

To the best of our knowledge, this study is the first to describe education and work interruption and resumption following the first diagnosis of HL in a large-scale international multicentre setting. Our study population consisted of long-term HL survivors from several European countries, across a period of four decades, including more than 1600 patients, which make it the largest study to date. Our findings showed that an interruption in education/work was common among HL survivors. However, the vast majority of those who interrupted their education or work were able to resume their activities within two years.

When looking at the HL survivors studying at the time of diagnosis, no significant associations for education interruption were found. Nevertheless, there was a trend towards declining interruption-rates throughout the study period, suggesting that less heavy treatment-regiments favours retention of activities (patients included in the later trials have generally been less heavily treated) [31]. Also, no significant associations for failure to resume education were

Table 1. Characteristics of the study population.

	Students		Workers	
	N	(%)	*N*	(%)
Total no. of patients	323	100	1323	100
Sex				
Male	134	(41.5)	713	(53.9)
Female	189	(58.5)	610	(46.1)
Age				
<18	91	(28.2)	0	(0.0)
18–29	228	(70.6)	546	(41.3)
30–39	2	(0.6)	435	(32.9)
40–49	1	(0.3)	247	(18.7)
≥50	1	(0.3)	95	(7.2)
Treatment year				
1965–1974	9	(2.8)	35	(2.6)
1975–1984	29	(9.0)	125	(9.4)
1985–1994	102	(31.6)	412	(31.1)
1995–2004	183	(56.7)	751	(58.8)
Country				
The Netherlands	152	(47.1)	598	(45.2)
France	112	(34.7)	518	(39.2)
Belgium	31	(9.6)	102	(7.7)
Other	28	(8.7)	105	(7.9)
Stage				
I	61	(18.1)	330	(24.9)
II	218	(67.5)	807	(61.0)
III or IV	44	(13.6)	185	(14.0)
Missing	0	(0.0)	1	(0.1)
Chemotherapy				
No	70	(21.7)	245	(18.5)
Yes	253	(78.3)	1078	(81.5)
Chemotherapy duration				
No chemotherapy	70	(21.7)	245	(18.5)
8–12 weeks	35	(10.8)	139	(10.5)
16–18 weeks	123	(38.1)	445	(33.6)
24 weeks or longer	95	(29.4)	491	(37.1)
Missing	0	(0.0)	3	(0.2)
Radiotherapy				
No	39	(12.1)	160	(12.1)
Yes	284	(87.9)	1163	(87.9)
(Any) relapse within 6 months from treatment start				
No	316	(97.8)	1309	(89.9)
Yes	7	(2.2)	14	(1.1)
Educational level				
No high school	NA		425	(32.1)
High school diploma	NA		462	(34.9)
University degree	NA		418	(31.6)
Missing	NA		18	(1.4)
Time since diagnosis (years)				
Median/Range/Q1–Q3	14.0/6.5-43.0/10.3-19.2		14.1/5.4-44.6/9.9-19.0	

Table 2. Resumption of education and work across a period of five years following the interruption.

	Resumption of education		Resumption of work	
Months	%	(95% CI)	%	(95% CI)
3	11.7	(7.6 – 17.8)	6.5	(5.1 – 8.2)
6	38.3	(31.3 – 46.2)	21.2	(18.8 – 24.0)
12	82.7	(76.5 – 88.1)	68.3	(65.3 – 71.2)
24	92.0	(87.1 – 95.5)	86.0	(83.7 – 88.1)
60	94.4	(90.2 – 97.3)	90.5	(88.6 – 92.3)

Patients who interrupted education and had information on education resumption available were included in the analysis of education resumption ($N = 162$). Patients who interrupted work and had information on work resumption available were included in the analysis of work resumption ($N = 961$).

identified. On the other hand, a positive association for education resumption was found for treatment with radiotherapy. However, this probably reflects that radiotherapy was the treatment of choice (for most of our study period) for patients with early-stage disease [36].

When looking at the HL survivors working at the time of diagnosis, work interruption was found to be significantly associated with female sex and country of residence, which likely reflects differences in labour market conditions across Europe. In the Netherlands for instance, the employer must pay at least 70% of a person's income for up to two years when the absence is due to illness [37]. In France on the other hand, the reimbursement is only 50% [38]. A difference, which unfortunately we could not adjust for.

Looking at resumption of work, several factors had to be considered. Comparable to our results, multiple studies concerning a broad spectrum of cancer patients also found higher age, female sex, and lower educational level to be negatively associated with return to work (RTW) [15,39–41]. Higher age being negatively associated with RTW could reflect that HL survivors approaching retirement would be more prone to leave the labour market. It has also been shown that the time it takes for cancer survivors to return to work is inversely proportional to age [2,42,43]. The effect of sex on RTW is not entirely understood, although it has been reported in many studies [13,15,40,44]. An explanation could be due to differences in employment rates between men and women. In Europe, the employment rate for men of the working age in general exceeds that of women by 11.7 percentage points [45]. It is also possible that the effect of sex reflects a sex wage gap disfavouring women across the EU [45,46]. If the differences between women's wages and sick leave compensation are smaller than for men, the incentive for women to RTW could be reduced. This is supported by findings from a French national cross-sectional survey involving 4270 cancer survivors that found that married men returned to work much faster than married women [46]. This may also explain why our results showed that women were more likely to interrupt their work in the first place. Furthermore, severe fatigue has been shown to be more frequent among female patients compared with male patients [47]. Regarding the negative correlation between lower educational level and RTW, it has been suggested that persons with a lower level of education more often have physically demanding works, and therefore may experience work limitations related to post-disease/post-treatment physical impairment [48–50]. Additionally, it has been speculated that employers and supervisors may be more willing to adjust for employees who are highly qualified and thus difficult to replace [51].

A systematic review of 64 original articles (primarily cross-sectional and longitudinal cohort studies) looking into employment and work-related issues in cancer survivors showed that overall, 63% (range 24–94%) of cancer survivors RTW, depending on the period of time after cancer therapy [39]. Similarly, an American study including 253 patients with breast, colon, lung and prostate cancer found that 67% were able to RTW five to seven years following their diagnosis [52]. Although the patterns of RTW can be diverse and complex to study [53], we found that long-term HL survivors fare quite well (92 and 86% of LSQ responders had returned to

Table 3. Association between survivors' characteristics and education and work interruption and resumption following HL diagnosis.

	Education interruption		Work interruption		Education resumption		Work resumption	
Covariate	OR (95% CI)	*p*-Value	HR (95% CI)	*p*-Value	HR (95% CI)	*p*-Value	HR (95% CI)	*p*-Value
Sex		0.554		<0.001		0.145		<0.001
Male	Ref		Ref		Ref		Ref	
Female	1.15 (0.72 – 1.82)		1.90 (1.44 – 2.51)		0.78 (0.56 – 1.09)		0.70 (0.61 – 0.80)	
Age		0.182		0.100		0.227		0.005
18–29			Ref				Ref	
30–39			0.99 (0.65 – 1.50)				0.85 (0.69 – 1.04)	
40–49			0.92 (0.56 – 1.52)				0.79 (0.61 – 1.02)	
≥50			0.54 (0.28 – 1.05)				0.62 (0.41 – 0.94)	
Less than 18 years	Ref				Ref			
18 years or older	1.43 (0.85 – 2.43)				1.29 (0.85 – 1.95)			
Treatment year		0.054		0.509		0.342		0.142
+ 10 years	0.70 (0.49 – 1.01)		0.93 (0.75 – 1.15)		0.89 (0.70 – 1.13)		1.08 (0.97 – 1.21)	
Country		0.192		<0.001		0.004		0.211
The Netherlands	Ref		Ref		Non-proportional hazards		Ref	
France	0.56 (0.28 – 1.12)		0.82 (0.55 – 1.22)				1.13 (0.92 – 1.37)	
Belgium	0.70 (0.25 – 1.97)		0.89 (0.44 – 1.77)				0.87 (0.61 – 1.23)	
Other	0.74 (0.24 – 2.24)		0.36 (0.19 – 0.66)				1.03 (0.69 – 1.53)	
Stage		0.751		0.865		0.575		0.015
I	Ref		Ref		Ref		Non-proportional hazards	
II	0.84 (0.41 – 1.74)		0.98 (0.67 – 1.44)		0.97 (0.58 – 1.64)			
III or IV	1.06 (0.37 – 3.00)		1.11 (0.61 – 2.00)		0.75 (0.37 – 1.53)			
Chemotherapy		0.621		0.125		0.774		<0.001
No	Ref		Ref		Ref		Non-proportional hazards	
Yes	1.17 (0.63 – 2.16)		1.34 (0. 92 – 1.95)		0.94 (0.60 – 1.47)			
Radiotherapy		0.874		0.541		0.030		0.057
No	Ref		Ref		Ref		Ref	
Yes	1.06 (0.51 – 2.20)		1.14 (0.75 – 1.73)		2.01 (1.07 – 3.78)		1.24 (0.99 – 1.55)	
Educational level				0.052				<0.001
No high school			Ref				Ref	
High school diploma			0.95 (0.63 – 1.42)				1.17 (0.95 – 1.43)	
University degree			0.68 (0.46 – 1.03)				1.50 (1.21 – 1.86)	

Estimates from a multivariate model including all covariates are presented.
For covariates with more than two categories, the confidence interval is adjusted for multiple testing using the Tukey–Kramer method.
Patients with data on all covariates available were included in the analysis of education ($N = 323$) and work ($N = 1304$) interruption. Patients who interrupted education and had information on all covariates and education resumption available were included in the analysis of education resumption ($N = 162$). Patients who interrupted work and had information on all covariates and work resumption available were included in the analysis of work resumption ($N = 947$).

education or work after two years, respectively). This is supported by findings from Horsboel et al. who showed in a Danish register-based cohort that the highest cumulative incidence of RTW among patients with haematological malignancies was observed for patients with HL (RTW proportion of 89–93% among 289 HL patients) [15]. However, younger age of HL survivors could be an important factor here, as RTW rates are generally higher in the adolescent and young adult population [8,54].

Although our results showed that most HL survivors will return to their education/work, only little is known about how they may manage the transition. This could be exceedingly relevant, as a diverse array of late effects has been documented in this surviving population [2,5,55]. In a study by Parson et al., approximately 30% of cancer patients reported difficulties 'keeping up with work or studies' more than 15 months after diagnosis [8]. Therefore (as suggested in a systematic review on physical and psychosocial problems in cancer survivors beyond RTW), health care practitioners, employers, co-workers, and insurance companies should be informed that diagnosis- and/or treatment-related problems may persist long after treatment has ended [56]. However, further research is needed to determine whether difficulties (e.g. impaired workability) after RTW apply to HL survivors as well.

One strength of our study is the unique dataset, which includes thousands of HL survivors from across Europe with a median follow-up of 14.0 years. By using the EORTC database combined with the LSQ we were able to evaluate outcomes given different combinations of treatment given in different time intervals. There are, however, certain limitations. As in all retrospective survivorship research, our data depend on self-reported outcomes which may have led to nonresponse- or recall bias. Nevertheless, recall bias should be limited as questions about significant life events (such as changes in occupation) are usually well memorised [9,13]. Also, a previous non-responders analysis found almost no differences in characteristics (including disease stage distribution) between those who returned the questionnaire and those who did not [27]. However, responders did tend to come from less recent trials. Also, responders had to some extent been treated with non-alkylating chemotherapy and radiotherapy above the diaphragm less often [27], which might influence external validity. Likewise, we cannot exclude attrition or survivorship bias. Furthermore, patients with co-morbidity and worse performance scores are often excluded from RCTs [57], and most of the HL survivors in our cohort had stage I or II disease at the time of diagnosis which could have led to over-optimistic estimates. However, both dose sizes and exposure to radiotherapy and/or chemotherapy have been reduced over time [31], which may have resulted in worse outcomes than would be obtained using more current treatment regimens [13]. Also, our sample of students was relatively small, resulting in rather wide

confidence intervals for this group. As a result, significant associations may not have been discovered. Finally, differences in legislations, social security systems and rehabilitation systems between countries could have influenced the results.

For many cancer patients, the ability to work not only represents financial benefits (including health insurance in some countries), but also having a purpose in life, a sense of contributing, control, normalcy, and distraction [51,58]. In fact, employment has been valued by cancer survivors as the third most important aspect of quality of life, following the ability to get out and to engage in social activities [56]. While quality of life is beginning to be routinely evaluated, comprehensive assessments of indices of return to work among HL survivors are not existing [50]. Our data provide important new insight into identification of vulnerable subgroups among HL survivors, findings that are crucial both from a clinical and a societal perspective. As a result, rehabilitation of HL survivors should not only focus on the medical aspects of surviving cancer, but also include education about the challenges some HL survivors may face in the labour market [50].

In conclusion, our data showed that long-term HL survivors (alive 5–44 years after diagnosis) commonly interrupted their education or work during treatment. However, more than 85% were able to resume their activities within two years. In this study, no associations between survivors' characteristics and failure to resume education were observed. Female sex, age $\geq$50 years and a lower level of education were found to be associated with not returning to work after HL treatment. As a result, aftercare programs should emphasise the effective transition of these vulnerable subgroups into the workplace following treatment.

Ethical approval

This study is exclusively register-based. All data are anonymized. In Denmark, register-based research (that does not include biological material) does not need to be notified to the scientific ethics committee system. Protocols and informed consent for the H1–H9 trials as well as the LSQ cross-sectional study was approved by local ethical committees in each participating country. The studies were conducted in accordance with the Helsinki Declaration. Participants who received the Life Situation Questionnaire have all consented to their responses being analysed.

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Data availability statement

Access to the data that support the findings of this study (request form) is available at https://www.eortc.org/data-sharing/. All data sharing takes place in accordance with EORTC's data sharing policy.

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