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Title Page

Post-treatment work patterns amongst survivors of lymphoma treated with high-dose chemotherapy with autologous stem-cell transplantation

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Abstract

Background This study describes post-treatment work patterns in lymphoma survivors treated with high-dose chemotherapy with autologous stem-cell transplantation (HDT-ASCT). It aims to identify determinants for labour force participation and exclusion after HDT-ASCT.

Methods Eligible patients were survivors of HDT-ASCT for lymphoma in Norway between 1995 and 2008, aged ≥ 18 years at HDT-ASCT. We divide survivors by current employment status (working (full vs. part-time) and unemployed). Main outcomes are current employment status, work hours and work ability. *Withdrawals* are patients who were employed when diagnosed but not before HDT-ASCT.

Results Of the 274 who completed the survey, 82% (N=225) were included in the final analyses. Mean age at survey was 52 years, 39% were female, 85% were employed when diagnosed, 77% before HDT-ASCT and 69% at survey. Employment before HDT-ASCT corresponds with a higher probability of employment at survey for a given symptom burden. In the most extensive statistical model, it increases with 37.3 percentage points. Work hours amongst withdrawals plummet after HDT-ASCT while work ability shows a rebound effect. The potential economic gain from their re-enter into the work force equals 2/3 of the average annual wage in Norway in 2012.

Conclusions For a given symptom burden, staying employed throughout diagnosis and treatment is associated with a higher probability of future employment. These results favour policies for labour force inclusion past diagnosis and treatment increasing cancer survivors' probability of future employment. However, we need more research on withdrawal mechanisms, and on policy measures that promote inclusion.

Background

High-dose chemotherapy with autologous stem-cell transplantation (HDT-ASCT) is a potentially curative treatment option for selected lymphoma patients. It is associated with severe acute and late adverse effects [1], causing physical and mental strain, and challenging patients' work ability. Most lymphoma patients treated with HDT-ASCT are within working age (18-67 years) when diagnosed, with potentially numerous years left until retirement. In a previous study, our group studied employment patterns and associated factors for this patient group [2]. We found psychosocial factors to be associated with labour market withdrawal at follow-up, but hardly any lymphoma-related variables. An extensive body of research relates to absenteeism in work life [3, 4], lending support to the hypothesis that (sickness) absence leads to more absence.

In this article, we describe work-related outcomes amongst lymphoma survivors treated with HDT-ASCT. We have access to data describing work life parameters in lymphoma survivors treated with HDT-ASCT before onset of illness,

during and after treatment. From this material, we also study post-treatment work patterns and try to identify determinants for stable labour force participation and exclusion post treatment.

The aims of the present study are to:

1. Investigate factors affecting labour force participation in lymphoma survivors after HDT-ASCT.
2. Compare work ability and work hours for withdrawals (patients who were employed when diagnosed but not before HDT-ASCT) and non-withdrawals.
3. Investigate the potential gain from re-entering those who withdraw into the labour force.

We postulate the following hypothesis using this dataset: Can withdrawal be “absorbing” and have a causal and negative effect on future labour supply.

Methods

Patients

The data source is a national multicentre cross-sectional follow-up study performed in 2012-2013 consisting of a detailed self-reported questionnaire [2, 5], results from a clinical examination [6], as well as data retrieved from patients’ charts and the clinical quality register for lymphoma at Oslo University Hospital (OUH). Survivors of HDT-ASCT, treated with BEAM (carmustine, etoposide, cytarabine and melphalan) as high-dose regimen for lymphoma in Norway between 1995 and 2008, aged ≥ 18 years at HDT-ASCT, alive at survey, residing in Norway and currently not undergoing systemic therapy for active malignancy were eligible (n=355, figure 1). Respondents who reported being students (n=3) or retired (n=40) at survey are excluded in the present study since the focus here is on work patterns before and after treatment and these two groups are not considered part of the formal labour force.

Treatment

Survivors are categorized according to primary lymphoma entity: Hodgkin lymphoma (HL), indolent non-Hodgkin lymphoma (NHL) and aggressive NHL, number of regimens prior to HDT-ASCT, and whether they experienced relapse after HDT-ASCT or not [2]. Body Mass Index (BMI) is from the clinical examination (kg/m²). We replaced 36 missing values using statistical measures based on self-reported BMI.

Main outcomes

Patients were asked to retrospectively report their employment status when first diagnosed and before HDT-ASCT, as well as their current work situation (at survey), according to eleven categories. We use this information to construct three

categories for employment status; fulltime workers (having a fulltime job, being self-employed, or on sick leave), part-time workers (part-time job), or not employed (unemployment insurance, disability insurance, temporary disability insurance, or homemaker).

Patients rated their work ability on a scale of 1 to 10 (where 10 is best), both as they perceived it when answering the survey, and how they remembered it before onset of illness (i.e. when first diagnosed). They were also asked to report the number of weekly work hours at survey and when diagnosed. Their *current employment status*, *current work hours* and *current work ability* are the main outcomes in our analyses.

Based on their current work situation (at the time of survey), we construct a three-part categorical variable for employment; full-time workers, part-time workers and not employed (table 1), and a binary variable for being employed at follow-up (not distinguishing between full and part time) or not.

Withdrawal from work life

We use the three questions that pin their employment status to three points in time (when diagnosed, before HDT-ASCT, and at survey) to create the tree shown in figure 1 to describe withdrawal from work life. We postulate that once you move from a blue box (inclusion) to a red box (exclusion) it is harder to return to a blue one. We refer to this as “withdrawal” from work life, conditioned on inclusion at the time of diagnosis, thus only defined for the left-hand side of the tree. Non-withdrawals are the respondents on the left branch of the left-hand side of the tree (three positives, n=125).

Fig. 1: Flowchart and tree showing who works when

Flowchart of the study and tree showing who works when diagnosed, before treatment and at survey (three time points). Withdrawal is defined as moving from a blue box (yes = inclusion) to a red box (no = exclusion). Deviances in sums due to missing values (8 total).

Pseudo panels for withdrawals and non-withdrawals

We exploit the variation in time from when a patient received HDT-ASCT and when he or she completed the questionnaire, and construct three intervals: 3-7 years, 8-12 years and 13 years or more. This way we create pseudo panels for current work hours and work ability, supplemented with work hours and work ability from when they were first diagnosed.

Ratios for work hours and work ability

We calculate ratios for work hours as *work hours in the withdrawal group* divided by *work hours amongst those who stayed employed from diagnosis to survey*, repeating the calculation for work ability.

Table 1: Descriptives

Variable description	Total (patients included in analyses)		Full-time workers	Part-time workers	Not employed
	N	Stats.			
N	225		113	40	68
<i>Current work situation (from questionnaire)</i>			<i>Fulltime job (94) Self-employed (18) Sickleave (1)</i>	<i>Part time job (40)</i>	<i>UI (2), DI (50) TDI (15) housewife (1)</i>
Background variables	<i>N (#225)</i>		<i>Statistics: Per cent</i>		
Female		39	21	63	54
Married	224	74	72	73	75
Higher education	224	47	51	54	37
			<i>Statistics: Mean (Std. dev.)</i>		
Age at diagnosis		40 (12.9)	39 (12.7)	40 (13.3)	42 (12.3)
Age at treatment		43 (12.9)	42 (12.3)	43 (14.0)	45 (12.6)
Age at questionnaire		52 (11.6)	51 (10.7)	52 (13.5)	54 (11.6)
Time: Diagnose to HDT-ASCT		2.9 (3.8)	2.9 (4.32)	3.1 (3.7)	2.7 (2.8)
Time: HDT-ASCT to survey		8.7 (3.7)	8.7 (3.8)	9.1 (3.7)	8.5 (3.6)
Labour market characteristics			<i>Statistics: Per cent</i>		
Employed at diagnosis		85	89	90	75
Employed before HDT-ASCT	221	77	91	79	53
Employed at survey	221	69	100	100	0
			<i>Statistics: Mean (Std. dev.)</i>		
Work hours at diagnosis	193	34 (13.3)	36 (12.2)	34 (11.0)	31 (14.6)
Work hours if employed now		21 (18.6)	34 (12.6)	21 (12.8)	0 (0)
Work ability at diagnosis	205	8.5 (2.8)	9.3 (1.5)	8.9 (2.7)	6.8 (3.9)
Work ability at survey	199	6.1 (3.2)	7.9 (2.1)	5.8 (2.0)	2.8 (2.9)
Health-related characteristics			<i>Statistics: Per cent</i>		
Heart disease	224	9	8	8	12
Other cancers		11	7	10	19
Relapse after HDT-ASCT		21	18	28	24
Chronic fatigue	224	33	21	43	49
Anxiety		21	12	18	37
Lymphoma diagnose					
➤ Hodgkin's lymphoma		27	28	25	26
➤ Aggressive lymphoma		65	65	70	62
➤ Indolent lymphoma		8	7	5	12
Treatment lines					
➤ One		28	33	23	21
➤ Two		59	54	63	65
➤ More than two		14	13	15	15

Table 1: Sample descriptives with sociodemographic and health variables and work-related characteristics. Deviancies due to missing values (of the 225 included in the final analyses, four had missing values for current work situation and could therefore not be categorised as full time, part time or not working).

Economic loss

We estimate an economic loss from the difference in work hours between the withdrawal group and the non-withdrawals, using wage statistics from Statistics Norway for 2012 by gender and level of education to estimate an expected mean wage for the withdrawal group.

Explanatory variables

We define marriage as being in a paired relationship, and higher education as more than 12 years of education. We construct two binary variables for somatic illnesses; one for having had one or more of three heart diseases (myocardial infarction, angina pectoris or heart failure), and another for second cancers (new cancer diagnosis, other than lymphoma). Chronic fatigue was assessed according to the Fatigue Questionnaire [7], containing 11 items concerning physical (7 items) and mental (4 items) fatigue during the last month. Two additional items cover duration and extent of fatigue. Responses are dichotomised (0 and 1 scored as 0, and 2 and 3 scored as 1), with CF defined as sum score of ≥ 4 of the dichotomised responses with duration of ≥ 6 months. Anxiety is derived from the Hospital Anxiety and Depression Scale (HADS), consisting of an anxiety and a depression subscale with seven items each [8]. Each item is scored from 0 (not present) to 3 (highly present), and anxiety caseness defined as a sum score of ≥ 8 on the anxiety subscale.

Statistical analyses

We run a multinomial logistic regression, allowing for comparison between more than two groups (table 2). The dependent variable was the categorical three-part variable divided into *not working* (base outcome), *part time (work)* and *full time (work)* at survey. We include six covariates, relaxing the rule of thumb of 10 events per variable in logistic regression [9]. The six covariates are employment before treatment (main variable of interest), gender and age at survey (necessary individual characteristics), and second cancers, chronic fatigue, and anxiety. We choose the latter three covariates based on their significance in the regression models (table 2).

We run five regression models with the binary variable for employment (i.e. employed or not) at follow-up as the dependent variable, conditioned on being employed at diagnosis (table 3). In model 1 employment before treatment is the sole covariate. We expand the model stepwise with sociodemographic variables (model 2), somatic health variables (model 3), mental health variables (model 4), and the number of treatment lines before HDT-ASCT and lymphoma type (model 5).

We use a standard t-test to test whether the difference in means between withdrawals' and non-withdrawals' work hours and work ability at more than 13 years is different from the difference in means at onset. We restrict the test to the

patients observed at diagnosis and 13 years or more after treatment. We test the null hypothesis, which assumes there is no difference in means.

Ethics

The South-East Regional Committee for Medical and Health Research Ethics (REC South East) approved the study, and all participants gave written informed consent.

Results

Attrition analysis

There are no differences between the participants and non-participants with regard to age at diagnosis, HDT-ASCT or survey, nor gender, observation time or lymphoma entity.

Patients characteristics

In total, 274 survivors completed the questionnaire (77% of eligible survivors), 49 were excluded, leaving 225 respondents for the final analyses (figure 1).

In total, 40% of the participants are female, 3 out of 4 are in a paired relationship, and about half have higher education. Their mean age was 40, 43 and 52 years at diagnosis, HDT-ASCT, and survey, respectively (table 1).

According to the labour market characteristics, 85% of the participants were employed when diagnosed, working on average 34 work hours per week. Their work ability averaged 8.5 out of 10. At survey, median 10.8 years later, the corresponding figures are 69%, 21 hours and 6.1 (table 1). The 99% confidence intervals show no overlap for the respective means.

Factors associated with being employed at survey

Results from the multinomial logistic regression model show that being employed before HDT-ASCT increases the probability of employment at survey, part or full time, compared to not being employed (base outcome) (table 2). The other covariates; female gender, higher age, diagnosed with second cancers, chronic fatigue and anxiety; reduce the probability of working full time at survey (coefficients < 1), while anxiety reduces the probability of working part time.

Table 2: Results from multinomial logistic regression

Variable description	Relative risk ratio	z	p-value	[95 % CI]	
Not working at survey (base outcome)					
Working part time at survey					
Employed before HDT-ASCT	4.17	2.82	0.005	[1.54	11.27]
Female	2.00	1.52	0.128	[0.82	4.88]
Age at survey	0.98	-1.28	0.200	[0.94	1.01]
Other cancers	0.39	-1.45	0.148	[0.11	1.40]
Chronic fatigue	0.98	-0.04	0.972	[0.40	2.40]
Anxiety	0.24	-2.49	0.013	[0.08	0.74]
Constant	-0.90	-0.10	0.922	[0.10	8.23]
Working full time at survey					
Employed before HDT-ASCT	9.57	4.66	0.000	[3.70	24.78]
Female	0.34	-2.68	0.007	[0.15	0.74]
Age at survey	0.95	-3.02	0.003	[0.92	0.98]
Other cancers	0.31	-2.13	0.033	[0.10	0.91]
Chronic fatigue	0.34	-2.65	0.008	[0.15	0.75]
Anxiety	0.32	-2.44	0.015	[0.12	0.80]
Constant	14.84	2.69	0.007	[2.08	106.07]

Table 2: Being employed before HDT-ASCT increases probability of employment at survey, part or full time, compared to not being employed (base outcome).

Employment before HDT-ASCT positively correlated with later employment

The main result from the five regression models (table 3) is that employment before HDT-ASCT is significantly and positively correlated with employment at survey throughout all five models. The constant in model 1 predicts a 33% probability of being employed at survey if *not* employed before HDT-ASCT, whereas being employed before HDT-ASCT adds 44.8 percentage points to this probability. In models two to five, employment before HDT-ASCT adds 44.5, 43.6, 38.4, and 37.3 percentage points, respectively.

Three other covariates are significantly and negatively correlated with employment at follow-up; having second cancers, anxiety, and being in a paired relationship. Results from the most extensive model (5) suggest that receiving a second cancer diagnosis reduces the probability of employment at survey by 47.4 percentage points. Anxiety is associated with a reduction in this probability of 19.2 percentage points, while being in a paired relationship is associated with a reduction of 14.3 percentage points. The remaining health variables have no significant effect on the probability of future employment.

Table 3: Results from the five regression models

Variable description	Model 1	Model 2	Model 3	Model 4	Model 5
N	184	183	182	182	182
Employed at survey	Yes	Yes	Yes	Yes	Yes
<i>Statistics: Each coefficient shows how the probability of employment at survey relates to the various covariates (* p<0.05; ** p<0.01; *** p<0.001; t-values in parentheses).</i>					
Constant	0.333*** (3.85)	0.701*** (3.70)	0.812** (3.20)	0.955*** (3.79)	0.962*** (3.71)
Employed before HDT-ASCT	0.448*** (4.83)	0.445*** (4.70)	0.436*** (4.62)	0.384*** (4.09)	0.373*** (4.00)
Female		-0.094 (-1.43)	-0.066 (-1.00)	-0.034 (-0.52)	-0.040 (0.60)
Married		-0.125 (-1.69)	-0.168* (-2.31)	-0.146* (-2.05)	-0.143* (-2.01)
Higher education		0.040 (0.63)	0.073 (1.20)	0.054 (0.90)	0.072 (1.18)
Age at survey		-0.005 (-1.63)	-0.004 (-1.36)	-0.005 (-1.82)	-0.004 (-1.15)
Body Mass Index			-0.005 (-0.71)	-0.004 (-0.57)	-0.006 (-0.91)
Heart disease			0.076 (0.66)	0.095 (0.83)	0.063 (0.55)
Other cancers			-0.444*** (-4.34)	-0.410*** (-4.09)	-0.474*** (-4.54)
Relapse			0.104 (1.30)	0.078 (0.98)	0.138 (1.65)
Chronic fatigue				-0.126* (-1.93)	-0.109 (-1.65)
Anxiety				-0.176* (-2.20)	-0.192* (2.40)
Treatment lines					
One					<i>(base outcome)</i>
Two					0.009 (0.13)
More than two					-0.168 (-1.57)
Lymphoma type					
Hodgkin					<i>(base outcome)</i>
Aggressive					-0.008 (0.09)
Indolent					-0.143 (-1.12)
Variation in model explained (%)	0.11	0.15	0.23	0.28	0.30

Table 3: Employment before treatment, conditioned on being employed at onset, stays significant throughout all five regression models (* p<0.05; ** p<0.01; *** p<0.001; t-values in parentheses).

Withdrawal versus non-withdrawal group

In figure 2 (top two panels), we show trajectories for the pseudo panels for work hours and work ability for non-withdrawals and withdrawals; their average reported weekly work hours at diagnosis were 38.2 and 34.5, respectively, similar to a regular workweek (37.5 hours). They rated their work ability at 9.2 (non-withdrawals) and 7.6 (withdrawals), on average. In the withdrawal group, average weekly work hours at survey drop to 7.1, 1.1 and 0 3-7, 8-12 and ≥ 13 years after HDT-ASCT, respectively. Work hours for non-withdrawals have a smaller drop, and stabilise at 30.5. Withdrawals' reported work ability at survey drops to 2.9 and 3, and increases to 5.1 in the same periods after treatment, while work ability for non-withdrawals drops steadily to 7.5, 7.1 and 7. The trajectory for work ability in the withdrawal group suggests a rebound effect over time.

Fig. 2: Pseudo panels for work hours and work ability

The two upper panels show pseudo panels for work hours and work ability, for withdrawals and non-withdrawals (always employed). Last panel shows rebound effect for withdrawals' work ability but not for their work hours. Ratios estimated as withdrawals' work ability (work hours) as share of non-withdrawals' work ability (work hours) from diagnose to survey.

Different trajectories: Testing differences in means

We amplify the differences in trajectories for withdrawals' and non-withdrawals in the last panel in figure 2. At diagnosis, work hours and work ability in the withdrawal group were around 90 and 80 per cent of non-withdrawals', respectively, but, while withdrawals' work hours drop to zero, work ability rebounds to a level similar to where it started 13 years or more after treatment (figure 2).

Results from the standard t-test show that the difference in means between withdrawals and non-withdrawals 13 years after treatment is significantly different from the difference in means at diagnosis for work hours ($\Pr(|T| > |t|) = 0.0001$), but not for work ability ($\Pr(|T| > |t|) = 0.265$). The difference in average weekly work hours is -5.4 hours at diagnosis, compared to -29.4 hours 13 years after treatment. Average work ability in the withdrawal group is 2.6 points lower at diagnosis, and 4 points lower after 13 years.

Economic loss estimation

The withdrawal group works on average 27 hours less per week than non-withdrawals at survey. Using wage statistics for 2012 (year of survey start) from Statistics Norway, by gender and level of education, we estimate an expected mean hourly wage of NOK 260. This gives us a yearly loss per person of more than NOK 300,000 (EUR 31,000), equivalent to 70 per cent of the average yearly wage in Norway in 2012 of NOK 470,900 (Statistics Norway).

Discussion

Our data suggest a strong correlation between withdrawing from the labour market during illness and future labour market prospects, even when controlling for an extensive set of health variables. This brings us back to our introductory hypothesis: Withdrawal is ‘absorbing’, and has a causal and negative effect on future labour supply. If our hypothesis holds true, there should be little or no change in the coefficient for employment before treatment (i.e. the opposite of withdrawal) as we expand the regression model with sociodemographic and health-related variables, and it should stay significant. This is precisely what we find. Thus, staying employed throughout diagnosis and treatment implies a consistently higher probability of future employment, regardless of symptom burden.

Our results are in line with other researchers’ findings on absenteeism; (sickness) absence leads to more absence, while being present (at work) promotes work participation. Studies using Norwegian administrative data, covering the whole population, show that compulsory dialogue meetings for long-term sickleave absentees reduced absence duration considerably [4]. Graded (instead of fulltime) sickleave had a similar effect, leading to shorter absence and higher subsequent employment rates [3]. The policy implications could be measures that promote inclusion throughout periods of illness and treatment, such as activity requirements [3].

Few studies have explored work life issues in long-term lymphoma survivors. A Danish registry-based study reported an increased risk of disability pension among survivors of haematological malignancies (including lymphoma) compared to the reference cohort [10]. In the patient cohort, comorbidity and need of treatment with anxiolytics and antidepressants after diagnosis were associated with disability pension. This is in line with our findings, and in line with a previous study by our group among young adult cancer survivors of different diagnoses, where late adverse effects and other health-related factors were negatively associated with work life issues [11].

These findings implicate a need for both health care workers and those working in the welfare system to be aware of late effects after cancer as factors associated with reduced work life participation. Interventions aiming at improving late effects after cancer are strongly needed, and might improve work participation in the long term.

Work hours and work ability decrease for both withdrawals and non-withdrawals from diagnosis, through treatment, until survey when the participants receive the questionnaire. However, whereas both work ability and work hours amongst non-withdrawals stabilise relatively quickly at a modestly lower level, the trajectories are different for those who withdraw from the labour market. Their work hours drop below 10 in the first years after HDT-ASCT and continue to fall. A decade later, they hardly work at all. Work ability also drops but the initial fall is smaller, and the trajectory suggests a catch-up effect 13 years or more after treatment. The question arises: Is the difference in work ability between

these two groups 13 years after HDT-ASCT identical to the difference that already existed at the time of diagnosis? And can the same be said for work hours? Does their withdrawal from work life stem not from lack of *ability*, but from lack of *possibility*?

Results from the standard t-test allow us to reject the null hypothesis for work hours, but not for work ability. We cannot conclude, on any conventional level of significance, that the difference in work ability 13 years after treatment is different from the difference in means that already existed at diagnosis, whereas for work hours it is highly significant. The ratios in figure 2 (last panel) illustrate this; while work ability for the withdrawal group starts just above 80 per cent, drops to 40 per cent, and rebounds to a level slightly below 80 per cent of non-withdrawals' work ability, their work hours drop from 90 to zero per cent of non-withdrawals'.

If anything, we expect work ability to be under-reported for respondents outside the labour force, due to self-justification bias, i.e. they under-report their work ability to justify their exclusion [12]. Thus, we consider the gap between work ability and employment a lower bound.

Work hours in the withdrawal group does not reflect the catch-up effect in work ability. Assuming we could avoid their withdrawal, what is the potential gain from re-entering these patients into the labour force? Our estimations suggest a yearly loss of NOK 300,000 (EUR 31,000), equivalent to 70 per cent of the average yearly wage in Norway in 2012 (Statistics Norway). Avoiding withdrawal and its subsequent effects could represent a substantial gain, not only for those directly affected but also for society as a whole.

Norwegian labour market characteristics

Compared to other European countries, Norway has a relatively high employment rate. On the other hand, a relatively high share of the working-age population receives health-related benefits [13]. Work force participation depends on individual characteristics, such as education and work ability, but also on labour market regulations and the income insurance system.

Strengths and limitations

Strengths of this study include the completeness and representativeness of the study population, with all lymphoma survivors after HDT-ASCT in Norway being accounted for, together with the high response rate of 77%. Furthermore, participants and non-participants are highly comparable, strengthening the generalisability of our results.

Our study is limited by the cross-sectional design preventing any conclusion regarding causality to be made. All work-related data were collected by questionnaire at one time point, with a risk for recall bias, and not controlled by interviews and/or data from The Norwegian Work and Welfare Administration.

Conclusion

In this national study, we find that Norwegian lymphoma survivors have a higher probability of employment after treatment with HDT-ASCT if staying employed throughout diagnose and treatment. Our results support the hypothesis that withdrawal from the labour market has a negative effect on future labour market participation, even as we control for an extensive set of health variables. Thus, for a given symptom burden, withdrawal negatively affects employment later in life.

Abbreviations

BEAM: Carmustine, etoposide, cytarabine and melphalan

BMI: Body Mass Index

EUR: Euros

HADS: Hospital Anxiety and Depression Scale

HDT-ASCT: High-dose chemotherapy with autologous stem-cell transplantation

HL: Hodgkin lymphoma

NHL: Non-Hodgkin lymphoma

NOK: Norwegian kroner

OUH: Oslo University Hospital

REC South East: Regional Committee for Medical and Health Research Ethics of South-East Norway

Declarations

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Competing interests: Kjersti Helene Hernæs (KHH) declares that she has no conflict of interest. Knut B. Smeland (KBS) declares that he has no conflict of interest. Unn-Merete Fagerli (UMF) has been on the Advisory Board for Roche and Takeda but declares that she has no conflict of interest in this study. Cecilie E. Kiserud (CEK) declares that she has no conflict of interest.

Authors' contributions: KHH contributed with the concept for the article, analysed and interpreted the data, made figures and tables, and wrote the main body of the manuscript. KBS contributed with conception and design of the study, collection and assembly of data, data analysis and interpretation, flowchart, attrition analysis and manuscript writing. CEK contributed with conception and design of the study, collection and assembly of data, data analysis and interpretation, and manuscript writing. UMF contributed with collection and assembly of data. All authors read and approved the final manuscript.

Ethics approval and consent to participate: The Regional Committee for Medical and Health Research Ethics of South-East Norway approved the study (2011/1353B). Informed consent was obtained from all individual participants included in the study. This article does not contain any studies with animals performed by any of the authors.

Availability of data: Data and material might be available upon request.

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Figures

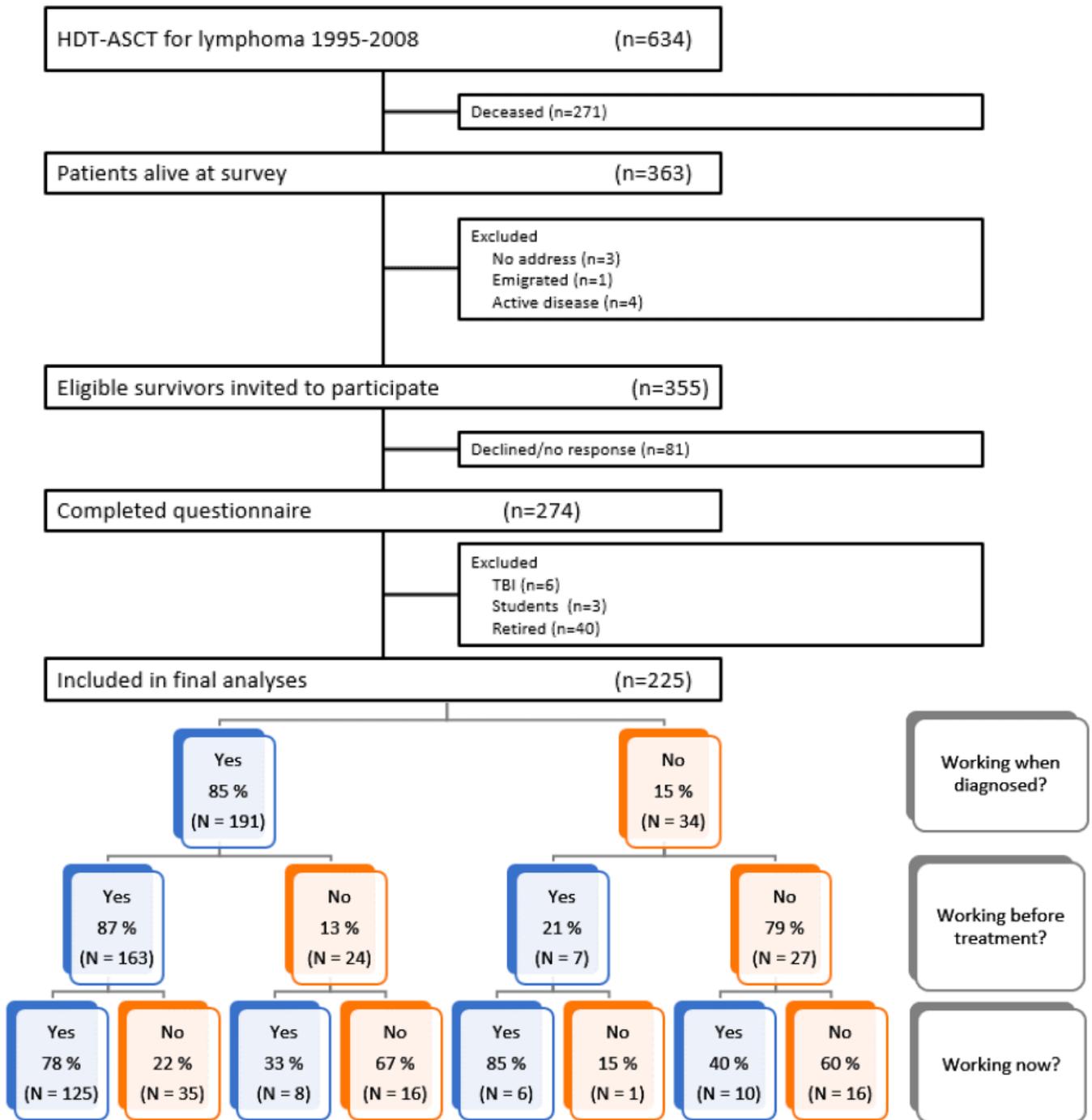


Figure 1

Flowchart and tree showing who works when diagnosed, before treatment and at survey (three time points). Withdrawal is defined as moving from a blue box (yes = inclusion) to a red box (no = exclusion). Deviances in sums due to missing values (8 total).

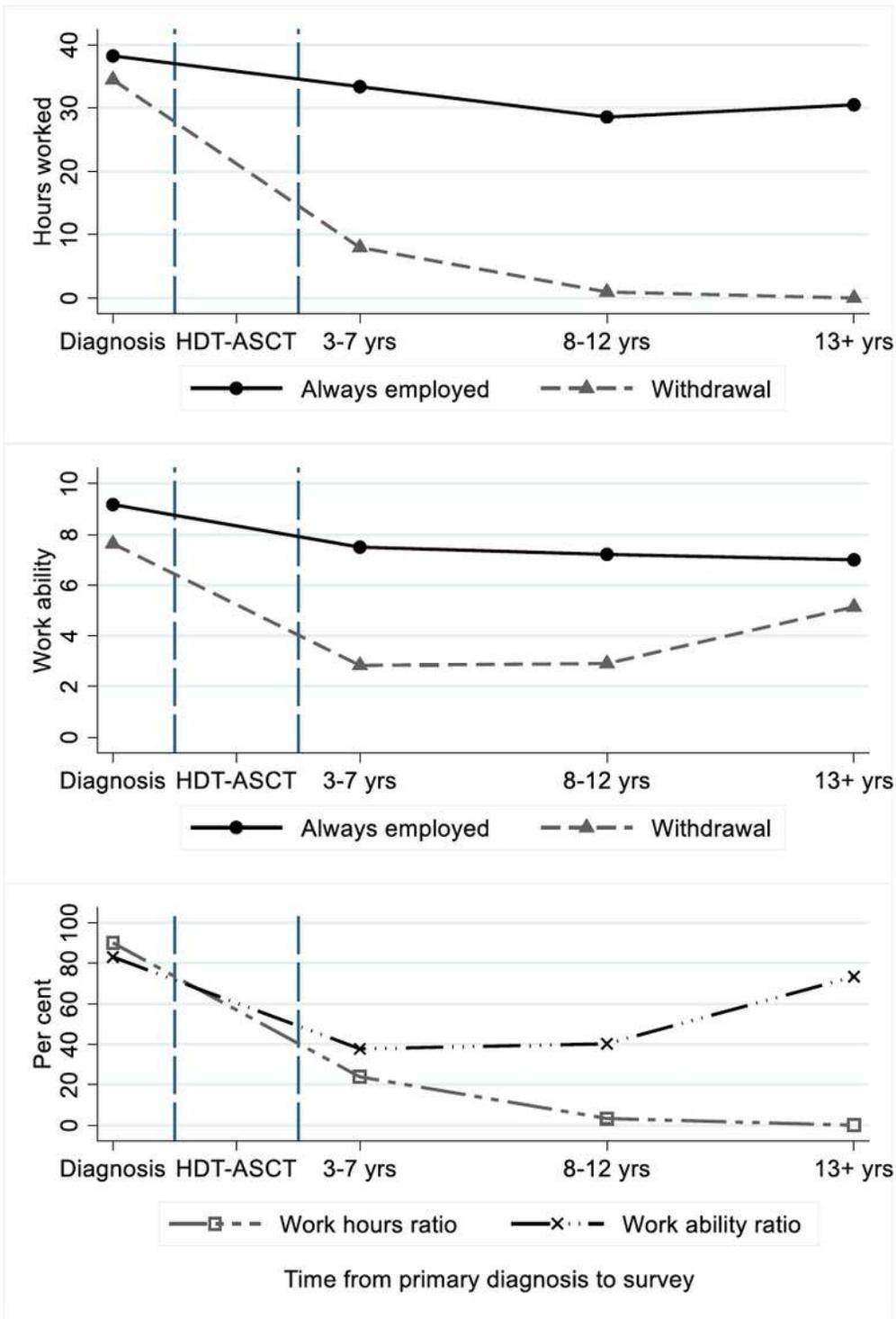


Figure 2

Pseudo panels for work hours and work ability