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Type of hematological malignancy is crucial for the return to work prognosis: a register-based cohort study

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Abstract
Purpose The aims of this study were to determine the proportion of return to work (RTW) among sick-listed patients diagnosed with one of eight subtypes of hematological malignancies; to evaluate the influence of type of hematological malignancy, comorbidity, use of anxiolytics and antidepressants, socioeconomic and demographic factors on RTW; and to investigate if these associations differ between genders.
Methods We combined data from national registers on all Danish patients diagnosed with hematological malignancies between 2000 and 2007. A total of 1,741 patients on long-term sick leave were followed until RTW, emigration, permanent withdrawal from the labor market, death, or February 2012, whichever came first.
Results A total of 1,140 (65 %) patients returned to work. A strong association was found between type of diagnosis and RTW ($p<0.001$), and the proportion of RTW was lowest for patients with multiple myeloma or acute leukemia compared to patients with Hodgkin lymphoma, diffuse large B-cell lymphoma, follicular lymphoma, chronic myeloid leukemia, and chronic lymphoid leukemia. Use of antidepressants or anxiolytics after diagnosis, gender, age, and educational level were also associated with RTW. Surprisingly, comorbidity was not associated with RTW ($p=0.94$); gender only modified the association between age and RTW.
Conclusion Two thirds of patients with hematological malignancies on sick leave RTW. A number of factors seem to lead to a poor prognosis, the hematological diagnosis being the most important, and these should be taken into account when performing studies on work outcome for patients with hematological malignancies.
Implications for Cancer Survivors Knowledge in this area should assist in identification of hematological cancer patients at risk of not returning to work so that early targeted rehabilitation interventions can be initiated.

Keywords Cancer epidemiology · Register-based · Cohort study · Hematological malignancies · Return to work

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Introduction

In recent years, treatment of hematological malignancies (leukemia, lymphoma, and multiple myeloma) has improved markedly resulting in an increased number of survivors [1]. More than one third of patients diagnosed with hematological malignancies are between 20 and 64 years of age [2]. Some will have difficulties returning to work life, affecting

the income of survivors and their families as well as potentially impacting on psychological and social well-being [3].

Studies have reported that patients with hematological malignancies are at increased risk of having work-related problems. Two Norwegian studies compared work outcome for survivors of different cancer types with cancer-free control groups. They found that 5 years after diagnosis, survivors from lymphoma had more sick leave compared with the control group [4], and that the probability of being employed after diagnosis was lower for survivors of leukemia and non-Hodgkin lymphoma compared to a control group [5]. Similarly, a Danish study found that patients with leukemia had a threefold increased risk and patients with non-Hodgkin lymphoma a twofold increased risk of disability pension compared to cancer-free controls [6]. Finally, previous studies have found that patients with hematological malignancies are among those at greatest risk of higher sickness absence, unemployment, and work-related disability in comparison to patients with solid tumors [7–9].

However, studies on work outcome for patients with hematological malignancies are sparse [10] and in all the above-mentioned studies, patients with these malignancies only comprised one to three minor subgroups of the total study population and diseases with different prognosis and treatment was grouped according to older classifications into "leukemias" and "non-Hodgkin-lymphomas".

Previous studies suggest that socioeconomic and demographic factors, work demands, diagnosis, and treatment as well as symptoms and functional level after cancer and treatment are potentially associated with work outcome for patients with hematological malignancies. The few existing studies have different conclusions and most of them have important methodological limitations [11]. If cancer patients at risk of not returning to work could be identified, early targeted interventions could be initiated in those patients at highest risk of work-related problems.

This register-based cohort study aimed to:

- Determine the proportions of return to work (RTW) among patients diagnosed with eight clinical relevant subtypes of hematological malignancies between 2000 and 2007 who were on long-term sick leave following diagnosis
- Evaluate the influence of type of hematological malignancy, comorbidity, use of anxiolytics and antidepressants, and socioeconomic and demographic factors on RTW
- Investigate if these associations differ between genders

Material and methods

Source population

In Denmark, the entire population has access to tax-financed health care. A considerable amount of health-related information is recorded in national population-based registers. Accurate and unambiguous linkage of register data at the individual level is possible by means of a unique civil registration number assigned to all Danish citizens [12, 13]. The study period proceeded from 1 January 2000 to 26 February 2012 within the entire Danish population of approximately 5.6 million inhabitants.

Identification of the study population

During a period from 1 January 2000 to 31 December 2007, we identified patients diagnosed with hematological malignancies in the Danish Cancer Registry. The registry contains data on the incidence of cancer in the Danish population since 1943; registration is carried out by multiple notifications from different data sources, which secures a high degree of completeness [12, 14]. Cases with hematological malignancies were identified according to the International Classification of Disease (ICD-10) and time of diagnosis. Information regarding morphology was also obtained. We categorized hematological malignancies into Hodgkin lymphoma (HL), diffuse large B-cell lymphoma (DLBCL), follicular lymphoma (FL), multiple myeloma (MM), acute leukemia (acute lymphoid leukemia (ALL)/acute myeloid leukemia (AML)), chronic myeloid leukemia (CML), chronic lymphoid leukemia (CLL), and others.

We only included patients at the age of 19–55 years, who had a job, and were on sick leave for more than 2 weeks within 12 weeks after diagnosis. Patients were followed until RTW, emigration, permanent withdrawal from labor market, death, or 26 February 2012, whichever came first.

Outcome

Denmark has a high level of social security and the main part of the welfare system is tax-financed. Social security covers the entire Danish population; if a citizen is not able to work due to physical or mental disability, the state is obligated to support the person financially through welfare benefits (sick leave benefits, disability pension, etc.).

In this study, information on welfare benefits was obtained from the Danish Register for Evaluation of Marginalisation (DREAM), which contains weekly information on welfare benefits at an individual level [15].

As regarding sick leave benefits, the threshold to enter DREAM between 2000 and 2007 was sick leave for more than two consecutive weeks, because the employer paid the first two consecutive weeks of sick leave. From the third consecutive week of sick leave, the employee was supported by tax-paid sick leave benefits registered in DREAM.

In this study, RTW was defined as the first period of four consecutive weeks without receiving sick leave benefits or other welfare benefits [16]. Patients who received unemployment benefits for at least 4 weeks were also considered to

have returned to work under the assumption that these individuals were capable of working. Information on death and emigration was also obtained from DREAM.

Demographic factors

Age at the time of diagnosis and gender were coded using the civil registration number and information on ethnicity was obtained from DREAM.

Socioeconomic factors

Information on family type, household income, educational level, and housing tenure was obtained from Statistics Denmark [17–19]. These data are updated once annually. We obtained information on educational level from 1 October the year before diagnosis; family type, household income, and housing tenure were assessed on 1 January at the year of diagnosis.

Use of anxiolytics or antidepressants

Use of anxiolytics or antidepressants was used as an indicator of mental health status following diagnosis. In order to investigate whether patients who were exposed to either anxiolytics or antidepressants after diagnosis developed a different RTW course than non-exposed patients, we obtained data on the prescription-based use of these drugs. Data was obtained from the Danish National Prescription Registry, which contains information on all dispensed prescriptions since 1994. These data include the type and amount of drug prescribed according to the Anatomical Therapeutical Chemical Classification System (ATC) and the date of drug redemption. Data are transferred from the pharmacies to the register, which thus includes all reimbursed drugs at the level of the individual user [20].

The ATC codes of interest for this study were antidepressants (N06A) and anxiolytics (N05B); it was registered if the patients were prescribed these types of medication during the first 3 years following diagnosis. Since we were only interested in the impact of exposure following hematological diagnosis, individuals to whom antidepressants or anxiolytics were prescribed the year before diagnosis, were considered non-users.

Comorbidity

Data on comorbidity was obtained from the Danish National Patient Register, which includes information on all hospital admissions in Denmark since 1977, as well as contacts to emergency rooms or outpatient clinics since 1995. Diagnostic information has been coded by physicians according to the ICD-10 codes since 1994 at each contact [12, 21, 22].

We computed a Charlson index score on the basis of the diagnoses recorded in the Danish National Patient Register for each patient in a 5-year period before diagnosis [23]. This index is considered to be a valid and reliable method to measure comorbidity [24]. A weight is assigned to define categories of co-morbid diseases and the index is the sum of these weights (from 0 to 6). Since we only had few patients with high levels of comorbidity prior to diagnosis, we classified comorbidity into only two groups according to the Charlson index score: 0 (no comorbidity) and >0 (comorbidity).

Statistics

The association between socioeconomic, demographic and clinical factors, and RTW was studied. Cumulative incidence curves were computed to illustrate the course of RTW according to type of hematological malignancy. By use of Cox proportional hazards regression, crude and adjusted hazard ratios (HR), and associated 95 % confidence intervals (CI) were estimated. The proportional hazards assumption was evaluated by assessing log-minus–log survivor curves. We used Wald tests to test the overall association between each independent variable and RTW.

In the first model, independent variables included diagnosis (HL, DLBCL, FL, MM, AML/ALL, CML, CLL, and others), comorbidity (0, 0<), gender (male or female), age (19–35, 36–40, 41–45, 46–50, or 51–55 years), highest attained educational level (basic school/high school, vocational education, or higher education), household income (low income, first quartile; middle income, second and third quartiles; and high income, fourth quartile), ethnicity (Danish citizens, immigrants or descendants from western countries, or immigrants or descendants from nonwestern countries), family type (single or couple, with and without children), and housing tenure (owner occupied, rental). The household income was given after taxation and adjusted for number of persons in the household with the following formula: household income/(no. of persons in household$^{0.6}$) [25].

In a second model, the same variables were included, but the analysis was stratified on gender. In order to test if gender modified the associations between independent variables and RTW, we incorporated gender interaction terms on all the other independent variables in the model. Wald test was then used to test for overall interaction between the genders and all the other independent variables. We also performed tests for interaction between gender and each of the other independent variables separately. Furthermore, we tested for gender interaction by using the first model and including an interaction term between gender and each of the other independent variables one at a time (without including other interactions).

The same steps were conducted with use of antidepressants or anxiolytics after diagnosis (entered as a time-

dependent variables and categorized as yes/no) as the main independent variable and adjusted for all covariates included in the first model. Death and permanent withdrawal from the labor market were considered as competing events to RTW in all the analyses.

Some of the hematological diagnoses (i.e., CLL or FL) might not result in sick leave immediately after diagnosis. However, due to the character of both disease and treatment, some of these patients will probably be sickness absent later on in the course. In recognition of this, we repeated the analyses extending the inclusion period to 3 years instead of 12 weeks in order to investigate if this had any impact on the results. Further, we examined if the results changed when we prolonged the 2 weeks sick leave inclusion criterion to 4 weeks. A last sensitivity analysis was performed in order to investigate the impact of the definition of RTW by repeating the analysis defining RTW as both 8 and 12 weeks without receiving welfare benefits.

Results

A total of 3,616 patients between 19 and 55 years (median age, 46 years; 42 % women and 58 % men) were diagnosed with hematological malignancies during the inclusion period. We excluded 979 patients as they were not active on the labor market at the time of diagnosis and another 896 patients were excluded as they were not on long-term sick leave following the diagnosis. Thus, a total of 1,741 patients on long-term sick leave were included in the study. The median age were 46 years ranging from 19 to 55 years; 41 % women and 59 % men.

RTW

Among the 1,741 patients who were on long-term sick leave, 1,140 patients (65 %) returned to work during the study period (Table 1). In all, 43 % returned to work during the first year, 60 % during the 2 years, and finally 64 % had returned to work after 4 years. Among those that did not RTW, 270 (16 %) died, 323 (19 %) left the labor market permanently, 1 (0.1 %) emigrated from Denmark, and 7 (0.4 %) were censured at the end of follow-up the period. For those that returned to work, the median time to RTW was 37 weeks (interquartile range, 21–57).

When excluding those who died, 77 % of the survivors returned to work (Table 1); 48 % during the first year after diagnosis, 70 % during 2 years, and finally 76 % had returned to work after 4 years.

Type of hematological malignancy

Figure 1 illustrates that the cumulative incidence of RTW differed by type of hematological malignancy. The highest incidence of RTW was found for patients with HL and the lowest for patients with MM and AML/ALL.

This was confirmed by the Cox regression analyses, where we found an association between diagnosis and RTW ($p<0.001$); RTW rates for patients with MM and patients with AML/ALL were lower than RTW rates for patients with HL (adjusted HR, 0.37; 95 % CI, 0.27–0.49 and adjusted HR, 0.44; 95 % CI, 0.36–0.54) (Table 2). The type of hematological malignancy was found to be associated with RTW for both men and women (Table 3).

Comorbidity and use of anxiolytics and antidepressants

No association was found between comorbidity and RTW ($p=0.94$; Table 2) and this was the case for both men and women (Table 3). The use of antidepressants or anxiolytics after diagnosis was found to be associated with RTW ($p<0.001$); thus, those who were prescribed antidepressants or anxiolytics within 3 years after diagnosis of hematological

Table 1 Patient outcome stratified by type of hematological malignancy

Diagnosis	*n* (%)	Emigrated *n* (%)	Permanent withdrawal *n* (%)	Dead *n* (%)	Followed until the end of study *n* (%)	RTW *n* (%[a]/%[b])
HL	289 (100)	0	19 (7)	13 (4)	1 (0.4)	256 (89/93)
DLBCL	293 (100)	0	35 (12)	42 (14)	1 (0.3)	215 (74/86)
FL	163 (100)	0	36 (22)	8 (5)	1 (0.6)	118 (72/76)
MM	195 (100)	0	98 (50)	35 (18)	0	62 (32/39)
AML/ALL	305 (100)	1 (0.3)	44 (14)	102 (34)	2 (0.7)	156 (51/77)
CML	79 (100)	0	20 (25)	4 (5)	1 (1)	54 (69/72)
CLL	84 (100)	0	15 (18)	5 (6)	0	64 (76/81)
Others	333 (100)	0	56 (17)	61 (18)	1 (0.3)	215 (65/79)
In all	1,741 (100)	1 (0.1)	323 (19)	270 (16)	7 (0.4)	1,140 (65/77)

[a] Proportion of RTW among the 1,741 included patients (death are considered as not returned to work)

[b] Proportion of RTW among survivors (those who died before they returned to work were excluded)

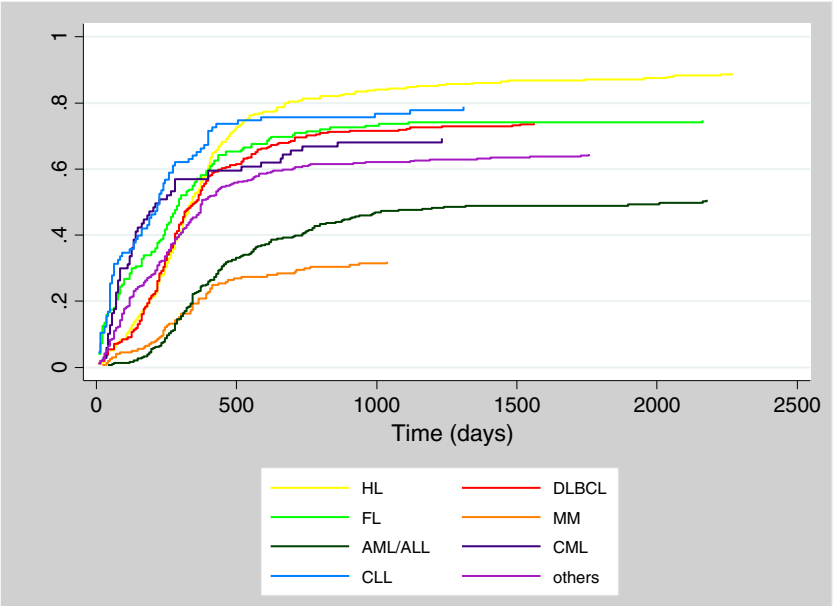

Fig. 1 Cumulative incidence of RTW by type of hematological malignancy (death and permanent withdrawal from labor market are considered as competing events)

malignancies were less likely to RTW compared to those who were not prescribed these types of medication (adjusted HR, 0.65; 95 % CI, 0.54–0.78). The same relationship was found when looking at the use of antidepressants (adjusted HR, 0.63; 95 % CI, 0.48–0.81) and anxiolytics (adjusted HR, 0.74; 95 % CI, 0.59–0.91) separately. Gender was not found to modify this association (data not shown).

Socioeconomic and demographic factors

Gender was found to be associated with RTW ($p<0.001$) as women had lower RTW rates than men (adjusted HR, 0.72; 95 % CI, 0.64–0.82; Table 2). There was a tendency that gender significantly modified the association between age and RTW ($p=0.03/0.20$). However, age was associated with RTW for both men ($p=0.02$) and women ($p=0.04$; Table 3).

Educational level also influenced the RTW rate ($p=0.007$) and patients with higher education had higher RTW rates than patients with vocational education (adjusted HR, 1.27; 95 % CI, 1.09–1.47; Table 2).

There was a tendency towards a positive association between household income and RTW, though not significant ($p=0.089$). Neither ethnicity nor family type or housing tenure was associated with RTW (Table 2).

Gender differences

The only association that was significantly modified by gender was the association between age and RTW, and this was just a tendency since we only found significant interaction when allowing for interaction between all factors and gender ($p=0.03$), whereas no association was found when allowing for interaction between only age and gender ($p=0.20$; Table 3).

Furthermore, no overall gender interaction was found ($p=0.09$), which also indicates that gender did not modify the associations between the independent variables and RTW in a considerable matter.

Sensitivity analyses

An additional 283 patients were included in the analyses when changing the inclusion period from 12 weeks to 3 years, and the proportion of RTW changed from 72 to 66 % for patients with FL and from 32 to 37 % for patients with MM. Other estimates remained unchanged (data not shown).

In the sensitivity analysis with 4 weeks of sick leave as inclusion criterion instead of 2 weeks, 1,629 patients were included. However, by and large, both absolute and relative estimates remained unchanged (data not shown).

When defining RTW as 8 and 12 weeks without receiving welfare benefits, the proportions of RTW decreased slightly; 65 % returned to work during the follow-up period when RTW was defined as 4 weeks without receiving welfare benefits. When prolonging the period to 8 and 12 weeks, the proportion of RTW was 64 and 62 %, respectively. Relative estimates remained almost unchanged (data not shown).

Discussion

In this nationwide register-based cohort study on RTW among 1,741 patients with hematological malignancies on long-term sick leave, we found that 65 % of the patients returned to work during the follow-up period. The type of diagnosis, use of antidepressants or anxiolytics after diagnosis,

Table 2 Cox proportional hazard regression analyses of RTW for the entire patient cohort

	N=1,741 (%)	HR_{crude} (95 % CI)	HR_{adj}[a] (95 % CI)	*p*
Diagnosis				
HL	289 (17)	1	1	<0.001
DLBCL	293 (17)	0.92 (0.77–1.10)	0.90 (0.74–1.09)	
FL	163 (9)	0.91 (0.73–1.13)	0.93 (0.73–1.17)	
MM	195 (11)	0.36 (0.27–0.47)	0.37 (0.27–0.49)	
AML/ALL	305 (17)	0.48 (0.39–0.59)	0.44 (0.36–0.54)	
CML	79 (5)	1.00 (0.75–1.34)	1.04 (0.77–1.41)	
CLL	84 (5)	1.20 (0.91–1.58)	1.21 (0.90–1.62)	
Others	333 (19)	0.87 (0.72–1.04)	0.85 (0.70–1.04)	
Comorbidity				
0	1,531 (88)	1	1	0.94
0<	210 (12)	0.97 (0.80–1.17)	1.01 (0.83–1.23)	
Gender				
Male	1,031 (59)	1	1	<0.001
Female	710 (41)	0.78 (0.69–0.88)	0.72 (0.64–0.82)	
Age				
19–35 Years	345 (20)	1.02 (0.82–1.23)	0.96 (0.78–1.17)	0.02
36–40 Years	213 (12)	1.10 (0.89–1.37)	0.95 (0.76–1.19)	
41–45 Years	285 (16)	1	1	
46–50 Years	360 (21)	1.19 (0.98–1.43)	1.08 (0.89–1.31)	
51–55 Years	538 (31)	0.92 (0.76–1.10)	0.79 (0.64–0.97)	
Educational level				
Basic school/high school	504 (28)	1.02 (0.88–1.18)	1.09 (0.94–1.26)	0.007
Vocational education	726 (42)	1	1	
Higher education	483 (29)	1.27 (1.11–1.46)	1.27 (1.09–1.47)	
Missing	28 (1)	–	–	
Household income				
Low (first quartile)	434 (25)	0.96 (0.83–1.10)	0.90 (0.77–1.05)	0.089
Medium (two to third quartiles)	868 (50)	1	1	
High (fourth quartiles)	434 (25)	1.09 (0.95–1.25)	1.12 (0.96–1.30)	
Missing	5 (0)	–	–	
Etnicity				
Danish	1,616 (93)	1	1	0.43
Western	67 (4)	1.09 (0.80–1.47)	1.09 (0.80–1.50)	
Nonwestern	58 (3)	0.79 (0.57–1.10)	0.81 (0.57–1.16)	
Family type				
Couple with children	795 (46)	1	1	0.26
Couple without children	490 (28)	0.87 (0.76–1.00)	0.97 (0.82–1.14)	
Single with children	85 (5)	0.85 (0.64–1.13)	1.14 (0.84–1.54)	
Single without children	366 (21)	0.84 (0.72–0.97)	0.86 (0.73–1.03)	
Missing	5 (0)	–	–	
Housing tenure				
Owner occupied	1,212 (70)	1	1	0.61
Rental	497 (28)	0.89 (0.78–1.01)	0.96 (0.83–1.12)	
Missing	32 (2)	–	–	

[a] All variables in the table are mutually adjusted

gender, age, and educational level were associated with RTW rates, and gender only modified the association between age and RTW significantly.

In previous studies, a wide range of proportions of RTW after cancer have been reported. In a systematic review on employment after cancer, a mean of 63.5 % of the participants (range, 24–94 %) managed to RTW depending on the period of time after cancer treatment [26]. Similarly, a Dutch study by Roelen et al. including 297 patients with leukemia and lymphoma found that 62 % of the patients had returned

Table 3 Cox proportional hazard regression analyses of RTW for the patient cohort stratified by gender

	Male				Female				Difference between male and female
	N=1,031 (%)	HR_{crude} (95 % CI)	HR_{adj}[a] (95 % CI)	*p*	*N*=710 (%)	HR_{crude} (95 % CI)	HR_{adj}[a] (95 % CI)	*p*	p^b/p^c
Diagnosis									
HL	163 (16)	1	1	<0.001	125 (18)	1	1	<0.001	0.20/0.51
DLBCL	193 (19)	0.97 (0.77–1.23)	1.05 (0.82–1.35)		101 (14)	0.80 (0.59–1.08)	0.73 (0.53–1.00)		
FL	86 (8)	1.08 (0.81–1.45)	1.15 (0.84–1.57)		77 (11)	0.77 (0.55–1.07)	0.67 (0.47–0.97)		
MM	108 (10)	0.42 (0.29–0.60)	0.46 (0.32–0.67)		87 (12)	0.28 (0.18–0.45)	0.24 (0.15–0.39)		
AML/ALL	181 (18)	0.51 (0.40–0.66)	0.48 (0.37–0.63)		124 (17)	0.42 (0.31–0.58)	0.38 (0.27–0.52)		
CML	42 (4)	1.37 (0.94–2.01)	1.44 (0.98–2.13)		37 (5)	0.70 (0.44–1.12)	0.70 (0.43–1.13)		
CLL	52 (5)	1.17 (0.82–1.67)	1.36 (0.92–1.99)		32 (4)	1.19 (0.78–1.83)	1.03 (0.65–1.63)		
Others	206 (20)	0.91 (0.72–1.15)	0.96 (0.75–1.24)		127 (18)	0.77 (0.58–1.04)	0.72 (0.52–0.98)		
Comorbidity									
0	897 (87)	1	1	0.55	634 (89)	1	1	0.70	0.50/0.21
0<	134 (13)	0.87 (0.68–1.10)	0.93 (0.72–1.19)		76 (11)	1.14 (0.84–1.55)	1.07 (0.77–1.48)		
Age									
19–35 Years	211 (20)	1.03 (0.80–1.31)	1.05 (0.80–1.37)	0.02	134 (19)	0.95 (0.71–1.27)	0.82 (0.59–1.13)	0.04	0.03/0.20
36–40 Years	125 (12)	1.13 (0.86–1.50)	1.01 (0.76–1.36)		88 (12)	1.04 (0.73–1.46)	0.84 (0.58–1.20)		
41–45 Years	150 (15)	1	1		135 (19)	1	1		
46–50 Years	212 (20)	1.06 (0.82–1.36)	0.95 (0.73–1.23)		148 (21)	1.35 (1.01–1.82)	1.28 (0.95–1.75)		
51–55 Years	333 (32)	0.85 (0.67–1.08)	0.70 (0.54–0.92)		205 (29)	0.95 (0.71–1.27)	0.93 (0.67–1.29)		
Educational level									
Basic school/ high school	293 (28)	1.06 (0.88–1.27)	1.12 (0.93–1.35)	0.01	211 (30)	1.00 (0.79–1.27)	1.04 (0.82–1.33)	0.42	0.65/0.41
Vocational education	470 (46)	1	1		256 (36)	1	1		
Higher education	245 (24)	1.46 (1.21–1.75)	1.34 (1.11–1.63)		238 (33)	1.19 (0.95–1.48)	1.17 (0.92–1.48)		
Missing	23 (2)	–	–		5 (1)	–	–		
Household income									
Low (first quartile)	265 (26)	0.85 (0.71–1.02)	0.79 (0.65–0.97)	0.03	169 (24)	1.13 (0.87–1.42)	1.14 (0.88–1.49)	0.28	0.092/0.081
Medium (two to third quartiles)	512 (50)	1	1		356 (50)	1	1		
High (fourth quartile)	250 (24)	1.01 (0.84–1.21)	1.07 (0.88–1.30)		184 (26)	1.24 (0.99–1.56)	1.20 (0.94–1.53)		
Missing	4 (0)	–	–		1 (0)	–	–		
Etnicity									
Danish	966 (94)	1	1	0.79	650 (92)	1	1	0.46	0.28/0.86
Western	36 (3)	1.05 (0.69–1.59)	1.03 (0.67–1.58)		31 (4)	1.16 (0.75–1.81)	0.19 (0.74–1.92)		
Nonwestern	29 (3)	0.86 (0.55–1.34)	0.85 (0.52–1.39)		29 (4)	0.76 (0.47–1.24)	0.77 (0.46–1.29)		
Family type									
Couple with children	476 (46)	1	1	0.21	319 (45)	1	1	0.97	0.63/0.18
Couple without children	270 (26)	0.82 (0.69–0.99)	0.92 (0.74–1.14)		220 (31)	0.96 (0.77–1.20)	1.00 (0.77–1.30)		
Single with children	25 (3)	0.81 (0.48–1.36)	0.97 (0.57–1.66)		60 (8)	1.02 (0.72–1.45)	1.10 (0.74–1.66)		
Single without children	256 (25)	0.76 (0.63–0.91)	0.80 (0.65–0.98)		110 (16)	0.92 (0.70–1.22)	1.03 (0.75–1.43)		
Missing	4 (0)	–	–		1 (0)	–	–		
Housing tenure									
Owner-occupied	722 (70)	1	1	0.18	490 (69)	1	1	0.58	0.21/0.065
Rental	287 (28)	0.83 (0.70–0.98)	1.14 (0.94–1.37)		210 (30)	0.99 (0.80–1.22)	0.93 (0.73–1.19)		
Missing	22 (2)	–			10 (1)	–	–		

[a] All variables in the table are mutually adjusted

[b] Wald test for interaction (between all factors and gender)

[c] Wald test for interaction (between gender and each independent variable one at a time)

to work 2 years after diagnosis [8]. This proportion is similar to the results of this present study, where 60 % returned to work during the first 2 years after diagnosis.

Previous studies have documented that patients with hematological malignancies are at increased risk of having work-related problems compared to cancer-free control groups [4–6] and patients with other cancer types [7–9]. In this study, we found that the type of hematological malignancy also was strongly associated with RTW rates. Patients with MM or AML/ALL had the lowest incidence of RTW, and they had considerable lower RTW rates than patients with HL. To the best of our knowledge, this is the first study on work outcome for patients with hematological malignancies that have been large enough to stratify data into more than four subtypes of diagnosis. In earlier studies, patients diagnosed with hematological malignancies only comprised one to four minor subgroups of the total study population; hematological malignancies with different treatment and prognoses were mixed. Thus, different diseases like CLL, CML, and acute leukemias has often been grouped together as "leukemias"; FL, DLBCL, and lymphoblastic lymphomas has been grouped under the term "non-Hodgkin lymphomas". This may make sense from a biological view, and from the view of a pathologist, but it makes little sense when you look at the diseases from the point of prognosis or treatment. Based on our results, there is a clear need to distinguish between different types of leukemia and different lymphoproliferative diseases. Our choice of grouping the types of diagnoses is of course debatable, but this study has been able to divide hematological malignancies into comprehensive subgroups and we have clearly shown that RTW is highly dependent on the type of hematological malignancy.

Surprisingly, we did not find an association between comorbidity and RTW. To the best of our knowledge, this has not been investigated in previous studies on patients with hematological malignancies and RTW. Carlsen et al. have evaluated the association between comorbidity and unemployment and early retirement pension for cancer patients in general, and they found that comorbidity was associated with the risk of early retirement pension but not with unemployment [6, 27].

We also found that when patients were prescribed antidepressants or anxiolytics after diagnosis, their RTW rates became lower than the RTW rates for patients to whom these types of medication were not prescribed. Only a few studies have investigated this association. An American cohort study by Syrjala et al. included 263 patients with different types of hematological malignancies treated with hematopoietic cell transplantation and did not find an association between self-reported symptoms of depression and RTW [28]. The presence of depression was measured using a validated self-reporting scale, which might explain the diverging results. In contrast, we only had information on exposure to antidepressants or anxiolytics, and hence, our data must be interpreted with caution. First of all, we must consider bias by indication as some of the patients might have been prescribed these drugs due to mental distress by getting a cancer diagnosis. Secondly, patients treated with either antidepressants or anxiolytics are not necessarily suffering from clinical depression or anxiety and this possible misclassification may have led to an overestimation of the actual number of patients with a clinical diagnosis of anxiety and depression. Therefore, the information on use of antidepressants or anxiolytics used in this study can only be interpreted as an indicator of mental health status, not as an expression of presence of clinical diagnoses of depression or anxiety.

We found that female gender, high age, and vocational education were associated with low RTW rates. No associations were found for household income, ethnicity, family type, and housing tenure. Results on the association between RTW and socioeconomic and demographic factors are diverging in other studies on patients with hematological malignancies. Still, in previous cohort studies, female gender has been shown to be associated with low RTW rates [11]. Unlike the present study, however, earlier cohort studies did not find an association between neither age nor educational level and RTW among patients with different types of hematological malignancies. The diverging results are most likely due to different patient populations. Hence, two of the studies are limited to mixed populations of patients with hematological malignancies treated with autologous or allogeneic hematopoietic cell transplantation [28, 29]; this is a small subgroup to the population in our study, which complicates a comparison. The picture is also unclear when considering studies on factors associated with RTW for patients with cancer in general. However, similar to our results, several studies found young age, higher education, and male gender to be positively associated with RTW [26].

Similar to our study, a recent published study found gender to modify the association between age and RTW among patients diagnosed with various cancer sites. In that study, however, gender was also found to have influence on the association between cohabitation status and RTW as married men returned to work faster than married women. Like in our study, gender was not found to modify the association between neither educational level nor income and RTW [30].

Strengths and limitations of the study

One of the strengths of our study is the use of population-based registries with complete follow-up. This enabled us to describe RTW among patients with hematological malignancies in a relatively large unselected population. The design was prospective allowing us to evaluate temporal associations and, further, all patients between the age of 19 and 55 diagnosed between 2000 and 2007 were eligible for inclusion. Finally, the fact that information on all the variables

was obtained through registers reduced the risks of recall and selection bias.

However, the study also has some limitations. First, we defined RTW as not receiving welfare benefits for four consecutive weeks. This definition might have caused misclassification of the outcome in the study, since we could have misclassified individuals as returned to work, if they were supported by their partner or parents at least 4 weeks following a period of sick leave. We do consider this as a rare scenario and we are aware that a possible misclassification will have caused an overestimation of the proportion of RTW in our study.

Another limitation is that the multivariable analyses were performed under the assumption that except for gender, there was no interaction between any other variables. It would have been relevant to perform analyses stratified on age groups and diagnoses. However, due to the limited number of individuals in each age group and diagnosis subgroup, we were not able to do this.

It is important to remember that this study focused on acute long-term sick leave following diagnosis. Long-term sick leave was here defined as 2 weeks of sick leave. This choice was conservative, i.e., as short as possible to include as many as possible with sick leave due to cancer. Sick leave periods shorter than 2 weeks were not registered in DREAM. However, the cause of sick leave is not registered in DREAM and some of the patients may have been listed as sick due to other reasons than cancer. Maybe such erroneous inclusion could have been reduced if longer sick leave periods had been used as inclusion criterion. However, we consider the risk of competing causes for 2 weeks sick leave as small within the 12 first weeks after cancer diagnosis. As mentioned earlier, some of the hematological malignancies causes sick leave for some of the patients later than within 12 weeks after diagnosis and these patients were not included in this study. However, our analyses with a prolonged inclusion period did not change the estimates.

Unfortunately, we had no access to data on disease status (complete or partial remission), which may also have an impact on work life. This was also the case for type of treatment; even though treatment clearly is related to the diagnosis, important associations may be overlooked. For instance, you would expect a difference in populations of patients with CLL or FL if there was a large difference in the use of aggressive first-line therapies versus a principle of wait and watch.

Similarly, we had no information on self-reported symptoms of late effects like physical impairments, fatigue, anxiety, and depression, which in several studies have shown to be endemic among patients with hematological malignancies [31–33]. Future studies might combine register-based data sources with data from questionnaires in order to explore the association between these factors and work outcome. Another task in future studies is to investigate work life situation for the entire population of patients with hematological malignancies, including those without a job at diagnosis. This could be done by determining the risk of long-term work disability in a cohort of patients diagnosed with hematological malignancies compared to a reference cohort without a history of these cancer types.

In conclusion, two thirds of patients with hematological malignancies on long-term sick leave RTW. A number of factors seem to herald a poor prognosis, the hematological diagnosis being the most important. These factors should be taken into account when performing studies on work-related issues in patients with hematological malignancies, and they may be exploited for early interventions aimed at RTW in this patient group.

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