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Socioeconomic inequalities in prognostic markers of non-Hodgkin lymphoma: Analysis of a national clinical database

Birgitte Lidegaard Frederiksen [a,*], *Peter de Nully Brown* [b], *Susanne Oksbjerg Dalton* [c], *Marianne Steding-Jessen* [c], *Merete Osler* [a]

[a] *Research Centre for Prevention and Health, Glostrup University Hospital, DK-2600 Glostrup, Denmark*
[b] *Department of Haematology, Copenhagen University Hospital, DK-2100 Copenhagen Ø, Denmark*
[c] *Institute of Cancer Epidemiology, Danish Cancer Society, Strandboulevarden 49, DK-2100 Copenhagen Ø, Denmark*

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ABSTRACT

The survival of non-Hodgkin lymphoma patients strongly depends on a range of prognostic factors. This registry-based clinical cohort study investigates the relation between socioeconomic position and prognostic markers in 6234 persons included in a national clinical database in 2000–2008, Denmark. Several measures of individual socioeconomic position were achieved from Statistics Denmark. The risk of being diagnosed with advanced disease, as expressed by the six prognostic markers (Ann Arbor stage III or IV, more than one extranodal lesion, elevated serum lactate dehydrogenase (LDH), performance status of two or more, presence of B symptoms and International Prognostic Index (IPI) of two or more), increased with decreasing level of education, in patients living alone, and in men. For instance, a significant decrease in the odds of being diagnosed with elevated LDH ($p = 0.02$), high performance status ($p = 0.004$), high IPI score ($p = 0.004$) and B symptoms ($p = 0.02$) was seen with higher level of education, whereas high stage of disease was significantly less likely in the higher educated (odds ratio [OR] = 0.85 (0.74–0.99)). The difference in risk seemed not to be mediated by differences in histological subgroups reflecting aggressiveness of disease among the social groups. One of the most likely mechanisms of the social difference is longer delay in those with low socioeconomic position. The findings of social inequality in prognostic markers in non-Hodgkin lymphoma (NHL) patients could already be implemented in the clinical practice if general practitioners (GP's) and physicians on hospitals paid special attention to patients with low educational level and unspecific symptoms.

1. Introduction

There seems to be social inequality in survival after most cancers, with less advantaged patients having the worst prognosis.[1,2] Few studies have documented such inequalities in survival in non-Hodgkin lymphoma (NHL) patients.[3–7] As the survival of NHL patients strongly depends on a range of prognostic factors like stage at diagnosis and performance status, the association between these prognostic factors and socioeconomic position (SEP) is of particular relevance in order to

* *Corresponding author:* Address: Capital Region of Copenhagen, Research Centre for Prevention and Health, Nordre Ringvej 57, Building 84/85, 2600 Glostrup, Denmark. Tel.: +45 43 23 32 83; fax: +45 43 23 39 77.
E-mail addresses: birfre02@glo.regionh.dk, blf@image.dk (B.L. Frederiksen).
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explain social differences in prognosis. However, to our knowledge previous investigations of the association between SEP and advanced stage have only included other types of cancer, e.g. breast, lung and colorectal cancer, showing diverging results but mainly increased risk of late-stage disease in persons with low SEP.[8–12]

Symptoms of NHL are generally rather unspecific, in particular for indolent sub-types, and may include fatigue, weight loss, fever, night sweats and swollen lymph nodes. Symptoms of NHL may be mixed up with symptoms of other chronic diseases, especially in patients with several comorbid disorders. In addition, characteristics such as the patients' awareness of their symptoms, an appropriate health behaviour (e.g. visiting the general practitioner (GP) for relevant symptoms) and good communication with health staff may impact on the time passed from the initial symptoms of NHL until the diagnosis and thus on the likelihood of being diagnosed with advanced disease. These characteristics may be more predominant among persons with high SEP, while comorbid disorders are more frequent among persons with low SEP.[13] This leads us to hypothesise that NHL patients with low SEP are diagnosed with more advanced disease than are those with high SEP; and further that education may be of greater impact than income, since the above mentioned characteristics presumably are more closely associated to education than to income, even though these SEP indicators are correlated.

Thus, in this study we investigate the association between three individual socioeconomic factors as well as comorbidity and a range of prognostic markers. The prognostic factors analysed are three indicators with relation to the progression of the disease: the Ann Arbor stage, the presence of extranodal involvement of the lymphoma, and elevated levels of lactate dehydrogenase (LDH), two indicators more closely related to the general condition and the symptoms of the patient: the Eastern Cooperative Oncology Group (ECOG) performance status[14] and the presence of B symptoms (fever, night sweats, and weight loss), and one composite measure: The International Prognostic Index (IPI) originally developed for aggressive lymphomas and a powerful and widely used tool in describing prognostic factors of NHL, which is generated from data on Ann-Arbor stage, performance status, extranodal lesions, LDH level and age.[15,16] We also investigate if social differences are mediated by differences in histological subtypes, reflecting the aggressiveness of disease, among social groups. Further, analyses are performed within the subgroup of patients diagnosed with diffuse large cell b-cell lymphoma (DLBCL), which is the largest subgroup, and belonging to one of the most aggressive subtypes of NHL cancer.

2. Materials and methods

2.1. Study population

The study population was derived from the Danish national lymphoma database, LYFO, which includes more than 90% of patients diagnosed in Denmark with *de novo* NHL.[17] The data are collected from questionnaires filled in by the medical doctors in all 13 haematological departments in Denmark, who diagnose and treat NHL. It is obligatory for all lymphoma-treating departments to report cases of lymphoma to the LYFO database. The database included 6596 persons born between 1920 and 1982 and diagnosed with NHL between 2000 through 2008. About 63 patients below the age of 25 were censored, since education and income of these young age groups does not reflect their true SEP. Further, a total of 362 persons (5%) for whom there were no achievable information on either highest attained education, cohabiting status, or disposable income 1 year prior to the diagnosis of lymphoma was excluded, leaving 6234 persons for analysis. Of these 2570 (41%) were diagnosed with DLBCL.

2.2. Outcome variables

A number of dichotomous outcome variables were defined based on data from the database describing presence or absence of the following prognostic markers: (i) Ann Arbor stage III or IV – indicating involvement of lymph node regions on both sides of the diaphragm muscle, (ii) more than one extranodal lesion, (iii) elevated serum LDH – above the reference value which depends on age, (iv) ECOG performance status of 2, 3 or 4 – indicating how the disease affects the daily living abilities of the patient, ranging from 0 'fully active without restrictions' to 4 ' completely disabled', (v) presence of B symptoms, and finally (vi) IPI of two or more – range from 0 to 5.

2.3. Exposure variables

The socioeconomic data were derived by linkage to the Central Population Registry and the population-based Integrated Database for Labour Market Research (IDA) in Statistics Denmark, by means of a unique personal 10-digit identifier, which is given to all persons residing in Denmark for more than 3 months.[18] Thus information on age, sex, cohabitation status, education and income was obtained for each patient. Cohabitation status was categorised as single and living with partner. Education was categorised in three groups, as short education (i.e. mandatory education of up to 7 and 9 years for patients born before and after 1st January 1958, respectively), medium education (between 8/10 and 12 years – latest grades of primary school, secondary school, and vocational education) and higher education (over 12 years). Income was defined as household income after taxation and interest per person, adjusted for number of persons in the household and deflated according to the 2000 value of the Danish crown (DKK). Yearly variation in income was accounted for by calculating the average income in the 5 years before the diagnosis.

A Charlson Comorbidity Index (CCI) was generated by linking the personal identification number to the files of the Danish National Patient Register.[19] Hereby full histories of diseases leading to hospitalisations and outpatient visits from 1978 and 1995, respectively, accumulated up to the year preceding the lymphoma diagnosis were obtained for each individual. The information in the Register includes dates of admission and discharge and diagnoses coded according to Danish modified versions of the ICD-8 and, from 1994, ICD-10.[20]

2.4. Other variables

Information on histological subgroups of NHL was retracted from the LYFO database and subtypes were grouped according

to aggressiveness and cell differentiation: diffuse large cell b-cell lymphoma and other high grade B-cell subtypes (DLBCL), follicular lymphomas and other indolent lymphomas (LOW), T-cell lymphomas (PTCL), mantle cell lymphomas (MCL) and lymphomas of unknown subtype (NHLNOS).

2.5. *Statistical methods*

Differences in the distribution of variables by level of education were analysed using the chi-square test. Multivariable logistic regression models were used to examine the influence of the socioeconomic factors and comorbidity on the various prognostic factors using the GENMOD procedure of SAS 9.1.3. Complete case analyses, excluding patients with unknown information on the outcome in question, were performed. Possible clustering within hospital departments were accounted for using generalised estimating equations. A three-step model was used. In the first model each socioeconomic or comorbidity variable was entered alone and adjusted for age, sex and year of diagnosis. In the second models the individual exposure variable was adjusted for variables more upstream in the causal pathway (education → cohabiting status → income → comorbidity) and in addition age, sex and year of diagnosis. In the final models analyses were adjusted for age, sex, year of diagnosis, level of education, cohabiting status, income and comorbidity. Since there were only minor differences in the estimates between the three models, only data from the final models are shown. Analyses were checked for colinearity, which was not found. Additionally, to explore whether social inequalities were mediated through a difference in aggressiveness of lymphoma among social groups, the histology subgroup variable was included in further models where relevant. For each model the odds ratio (OR) and 95% confidence intervals (CI) were calculated. All tests were two-sided. Investigations of interaction between SEP and sex, comorbidity, and age below or above 65 (the typical age of retirement), respectively, as well as between comorbidity and sex, and age below or above 65, respectively, were performed, but not found. Furthermore, interaction analyses between education and sex restricted to the elderly above 65 years of age were performed, and no interactions found. Analyses were repeated in the subgroup of DLBCL patients.

3. Results

The mean age of the 6234 patients was 64 ± 12 years (mean ± SD) and 55% were males. Patients with short education were older, more likely female, living alone, had lower income and higher comorbidity scores than patients having a higher education (Table 1). Further, those with short education had higher Ann Arbor stage, performance status and IPI score, while they did not differ from patients with higher education regarding extranodal involvement, LDH, and B symptoms. Patients with short education were more likely to have the more aggressive subtypes of NHL, the DLBCL.

The multivariable analyses showed significant impact of level of education, cohabitation status and sex on the prognostic indicators (Table 2). A significant decrease in the odds of being diagnosed with elevated LDH (OR = 0.83 (95% confidence interval 0.74–0.93) in higher versus short educated, p, trend = 0.02), high performance status (OR = 0.62 (0.53–0.72), p, trend = 0.004), high IPI score (OR = 0.74 (0.62–0.89), p, trend = 0.004) and B symptoms (OR = 0.77 (0.69–0.86), p, trend = 0.02) was seen with higher level of education, whereas high stage of disease was significantly less likely among those with a higher education (OR = 0.85 (0.74–0.99)). Income was not associated with any prognostic factor. Furthermore, women had lower odds of being diagnosed with high stage disease (OR = 0.83 (0.71–0.97)), two or more extranodal sites involved (OR = 0.85 (0.77–0.93)), and a high performance status (OR = 0.83 (0.73–0.94)) than did men. Patients living alone had higher odds of being diagnosed with high stage disease (OR = 1.17 (1.03–1.33)), two or more extranodal sites involved (OR = 1.19 (1.06–1.33)), high performance status (OR = 1.31 (1.11–1.54)) and high IPI score (OR = 1.25 (1.16–1.34)), than did those living with a partner. Furthermore, high comorbidity was association with high performance status as expected (OR = 1.69 (1.31–2.19) in CCI $\geqslant$ 2 versus CCI none, p, trend = 0.006). Also, a decrease in the odds of advanced stage was seen with increasing number of comorbid conditions, however, not significant (OR = 0.85 (0.70–1.02) in CCI $\geqslant$ 2 versus CCI none, p = 0.07). Comorbidity was not associated with the other prognostic factors.

Adjustment for histological subgroup, reflecting aggressiveness of disease, caused only negligible changes in the estimates. Thus, histological subgroup did not seem to mediate the social gradient.

We repeated all the above analyses in the 2564 DLBCL patients and found similar trends in the point estimates; however, confidence intervals were wider and therefore of less significance. Yet, no associations between sex and the prognostic factors were found (data not shown).

The patients censored, due to missing information on socioeconomic data (mainly education and income data) did only differ from those included in the study with regard to B symptoms and level of LDH. Sensitivity analyses revealed that ascribing these patients to low education and income, which is the most realistic setting, strengthened the associations to education slightly and vice versa. Also, sensitivity analyses including the 496 patients with missing information on IPI strengthened respectively attenuated the association between education and IPI only marginally.

4. Discussion

This is the first study to examine the association between socioeconomic position and prognostic factors in patients diagnosed with NHL. Our main finding was that the risk of being diagnosed with advanced disease, as expressed by six prognostic markers, increased with decreasing level of education, and in patients living alone. This difference in risk seemed not to be mediated by differences in histological subgroups reflecting aggressiveness of disease among the social groups. We also found that men were diagnosed with more advanced disease compared to women.

Our study has both strengths and limitations. Firstly, our database has a high coverage including more than 90% of NHL patients diagnosed in the study period and is based on registrations from a whole nation, thus minimising selection

Table 1 – Baseline characteristics of 6234 non-Hodgkin lymphoma patients, born 1920–1987, Denmark, 2000–2008.

	Total		Short education	Medium education	Higher education	*p*
	n	%	%	%	%	
Level of education						
Short (only mandatory, 7/9 year)	2081	33.4				
Medium (8/10–12 year)	2930	47.0				
Higher (>12 year)	1223	19.6				
Disposable income						<0.0001
Lowest (1st quartile)	1509	24.2	40.7	19.6	7.2	
2nd quartile	1557	25.0	29.7	26.4	13.5	
3rd quartile	1573	25.2	19.6	28.0	28.2	
Highest (4th quartile)	1595	25.6	10.1	25.9	51.1	
Cohabiting status						<0.0001
Living with partner	4383	70.3	64.0	72.9	75.0	
Single	1851	29.7	36.0	27.1	25.0	
Sex						<0.0001
Men	3421	54.9	47.4	58.6	58.5	
Women	2813	45.1	52.6	41.4	41.5	
Charlson Comorbidity Index						<0.0001
None	4177	67.0	61.2	68.3	73.8	
1	1026	16.5	19.0	16.2	12.8	
2	595	9.5	11.0	8.5	9.7	
$\geqslant 3$	436	7.0	8.8	7.0	3.8	
Age (years)						<0.0001
25–39	236	3.8	1.6	4.6	5.6	
40–49	549	8.8	3.6	10.6	13.4	
50–59	1410	22.6	12.9	27.1	28.5	
60–69	1824	29.3	30.7	28.7	28.3	
70–79	1722	27.6	39.0	22.8	19.8	
80–89	493	7.9	12.2	6.3	4.5	
Year of diagnosis						0.001
2000–2002	1844	29.6	32.4	28.4	27.6	
2003–2005	2147	34.4	34.7	34.5	33.7	
2006–2008	2243	36.0	32.9	37.1	38.7	
Ann Arbor stage						0.002
1	1425	22.9	22.0	22.5	25.3	
2	715	11.5	11.1	11.5	12.0	
3	1021	16.4	15.5	17.5	15.2	
4	2890	46.4	47.5	45.9	45.6	
Unknown	183	2.9	4.0	2.6	1.9	
Two or more involved extranodal lesions						0.21
Yes	1076	17.3	18.5	16.7	16.7	
No	5158	82.7	81.6	83.3	83.3	
Elevated level of lactate dehydrogenase (LDH)						0.59
Yes	2245	37.7	38.0	38.1	36.4	
No	3707	62.3	62.0	61.9	63.6	
Missing	282	–				
The Eastern Cooperative Oncology Group (ECOG) performance status						<0.0001
0	3248	52.7	44.7	54.0	62.8	
1	1848	30.0	32.8	30.4	24.1	
2	539	8.7	11.5	8.2	5.4	
3	319	5.2	6.3	4.4	5.0	
4	215	3.5	4.7	3.0	2.6	
Missing	65					
International Prognostic Index (IPI) score						<0.0001
Low (0–1)	2124	37.0	28.9	39.8	43.6	
Low-intermediate (2)	1816	31.7	32.7	31.4	30.6	

(*continued on next page*)

Table 1 – (*continued*)

	Total		Short education	Medium education	Higher education	*p*
	n	%	%	%	%	
High-intermediate (3)	1129	19.7	22.4	18.9	17.2	
High (4–5)	669	11.7	16.1	9.9	8.7	
Missing	496					
B symptoms						0.07
Yes	2268	37.4	38.6	37.8	34.7	
No	3791	62.6	61.4	62.2	65.4	
Missing	175					
Histological subtype						0.001
Diffuse large cell b-cell lymphoma (DLBCL)	2670	42.8	45.2	42.1	40.5	
Other indolent lymphomas (LOW)	2490	39.9	37.0	40.7	43.3	
Mantle cell lymphomas (MCL)	341	5.5	6.0	5.4	4.9	
Lymphomas of unknown subtype (NHLNOS)	319	5.1	6.2	4.8	4.0	
T-cell lymphomas (PTCL)	414	6.6	5.7	7.1	7.3	

of special groups of patients. Six percent of the primary population was excluded due to missing information on socioeconomic variables, and 8% had missing information on IPI, however, the sensitivity analyses showed that this could not affect the results considerably. Given the recognised similarities between the Danish society and health care system and the other Northern European countries in both financing and delivery of health care, our results may be extrapolated to those countries, while validation using data from countries with different health care systems may be required. Secondly, our analyses were done using individual data on SEP, hereby reducing misclassification of exposure which arises when using area-based measures of SEP.[21] Further, SEP data were achieved from central registers, which collect data prospectively and for administrative purpose, thus, eliminating recall bias as often seen when using SEP data based on self-report.[22] We used income as one of our SEP indicators. The income variable may be prone to reverse causality; it is possible that NHL patients, due to fatigue and other symptoms affecting their ability to work, experience a decrease in income. We tried, however, to take account of this by calculating the average income of the 5 years preceding the year of the NHL diagnosis. Thirdly, we used a measure of comorbidity based on Charlsons Comorbidity Index.[19] Although the CCI is a thoroughly validated and widely used tool to handle comorbidity, it is a relatively crude measure, which does not differentiate between the mildest and the most severe cases within the included categories of diseases. Furthermore, our CCI was based on hospital discharge and outpatient visit diagnosis only, thus, patients with comorbidity treated in general practice only were registered with zero comorbidity. This may lead to misclassification of exposure and residual confounding. Finally, and perhaps most importantly, although our study shows that short education, living alone and being a man is associated with more advanced disease at the time of diagnosis, we were unable to explore the mechanisms behind these differences in depth. Information on the time point of symptom onset, first visit at the GP, first visit at the haematological department and waiting time on diagnostic procedures would have been valuable in the search for the underlying mechanisms. Unfortunately, this information was not available.

While a handful of studies have shown an association between aggregate or individual indicators of SEP and survival in NHL[3–7], the direct relation between SEP and prognostic factors of NHL has only been reported in univariate analyses in one of these studies.[6] In that study including 1743 Scottish patients deprivation as measured by the Carstairs score based on the patients' area of living was associated with more B symptoms and poorer performance status, but not with other indicators of more advanced disease.

Deprivation has been associated with more advanced stage of disease in other cancer types, including breast, colorectal, cervical, ovarian, prostate and lung cancers, although evidence is not unambiguous.[8–12] These cancers are generally dominated by more obvious symptoms than is NHL and some of these cancers are screened for in population screening programmes. The mechanisms behind social inequalities in the progression of disease may thus be different in NHL patients and these other cancer patients, and the results from these investigations should not be extrapolated to NHL.

Our finding that education, not income, was associated with the prognostic factors is in accordance with our hypothesis that education has a greater impact on the patients' ability to interpret signs and symptoms appropriately and react in a timely way. This may affect the time passed from the initial symptoms of NHL until the first contact to the health care system, the patient delay. Further, the well-educated patient may have a better communication with the GP, which may facilitate how the GP explores and takes action on the patient's history – affecting GP delay. Also, one might hypothesised that, even though Denmark has a tax-financed healthcare system with free access to medical advice and treatment in general practices and hospitals, the educated patients may be able to gain faster access to the health care system, minimising delay with relation to the diagnostic process and the treatment. The literature regarding SEP and delay, measured as the number of days of delay in the patient pathway, is sparse, and few studies include NHL patients, showing no clear inequality.[23,24] The finding that living alone was associated with more advanced disease may also be related to delay; spouses urging those with a partner to seek medical help. Another possible explanation of the social

Table 2 – Adjusted odds ratios (with 95% confidence intervals) of six prognostic markers of survival among persons diagnosed with non-Hodgkin lymphoma in Denmark, 2000–2008.

No. events/no. included	Ann Arbor stage III, IV 3911/6051			Two or more extranodal lesions 1076/6234			Elevated level of LDH 2245/5952			Performance status > 2 1073/6169			IPI ⩾ 2 1798/5738			B symptoms 2268/6059		
	OR	LCL	UCL	OR	LCL	UCL	OR	LCL	UCL	OR	LCL	UCL	OR	LCL	UCL	OR	LCL	UCL
Sex																		
Male	1			1			1			1			1			1		
Female	0.83	0.71	0.97	0.85	0.77	0.93	1.11	1.01	1.21	0.83	0.73	0.94	0.89	0.78	1.01	0.94	0.84	1.06
Cohabiting status																		
Living with partner	1			1			1			1			1			1		
Single	1.17	1.03	1.33	1.19	1.06	1.33	1.05	0.94	1.17	1.31	1.11	1.54	1.25	1.16	1.34	0.99	0.92	1.05
Level of education																		
Short education	1			1			1			1			1			1		
Medium education	0.99	0.84	1.16	0.91	0.75	1.10	0.94	0.83	1.06	0.74	0.65	0.84	0.83	0.75	0.91	0.92	0.81	1.05
Higher education	0.85	0.74	0.99	0.90	0.78	1.05	0.83	0.74	0.93	0.62	0.53	0.72	0.74	0.62	0.89	0.77	0.69	0.86
	p, trend = 0.10						*p*, trend = 0.02			*p*, trend=0.004			*p*, trend = 0.004			*p*, trend = 0.02		
Disposable income																		
Lowest (1st quartile)	1			1			1			1			1			1		
2nd quartile	0.93	0.82	1.05	0.98	0.78	1.21	1.03	0.88	1.21	0.99	0.79	1.25	1.03	0.85	1.25	1.05	0.95	1.16
3rd quartile	0.92	0.81	1.04	1.01	0.83	1.22	1.07	0.94	1.22	0.94	0.83	1.07	1.14	1.02	1.28	1.09	0.96	1.23
Highest (4th quartile)	1.03	0.86	1.24	0.93	0.76	1.14	1.12	0.96	1.31	1.03	0.88	1.21	1.08	0.90	1.31	1.11	0.97	1.28
Charlson Index																		
None	1			1			1			1			1			1		
1	0.87	0.79	0.97	0.84	0.68	1.05	1.01	0.85	1.19	1.20	0.89	1.61	1.02	0.85	1.23	1.03	0.90	1.18
⩾2	0.85	0.70	1.02	0.95	0.74	1.22	1.00	0.85	1.19	1.69	1.31	2.19	1.11	0.96	1.29	0.93	0.81	1.06
	p, trend = 0.07									*p*, trend = 0.006								

All analyses are adjusted for age, sex, cohabiting status, year of diagnosis, level of education, disposable income, Charlson Comorbidity Index. Analyses are controlled for clustering at the department level. *p*-values (trend) are not shown if above 0.10.

Abbreviations: LCL, lower confidence limit; UCL, upper confidence limit.

gradient would be that patients with low SEP had more aggressive disease or a poorer host response than high SEP patients. However, intuitively this mechanism would involve an income gradient, in addition to the found educational gradient, since income affects nutritional status and living conditions which may again affect immunocompetence.[25] This was not found. Furthermore, adjustment for subtype of NHL, as a marker of disease aggressiveness, did not influence the difference in the risk of advanced disease among educational and cohabiting groups. Thus, we did not find much support for this mechanism.

Comorbidity, as measured by a CCI based on in- and outpatient hospital discharge diagnosis, was not associated with advanced disease, except for the expected positive association with performance status. A non-significant trend ($p = 0.07$) of reduced risk of high Ann Arbor stage with increasing number of comorbid conditions may however suggest that multimorbid patients who are in regular contact with hospital staff and consequently may have easier access to diagnostic facilities have shorter delay. However, since this finding was confined to only one prognostic variable, the interpretation should be regarded with much caution.

The different prognostic variables used in this study reflect different dimensions of the advancement of disease and some may have slightly different interpretation among NHL subgroups. While Ann Arbor stage, performance status and B symptoms are equally important among the different subgroups, 'two or more extranodal lesions' is more important as prognostic factor among DLBCL patients, than among some minor subgroups, like cutaneous NHL and marginal zone tumours, which are extranodal per definition. Our subanalyses of DLBCL patients support the results of more advanced disease among patients with low SEP.

5. Conclusions and implications

Our findings suggest that higher level of education, living with a partner, and being female is associated with reduced risk of being diagnosed with advanced disease of NHL. One of the most likely mechanisms of the social difference is longer delay in those with low SEP. Systematic investigations of which phases of the clinical pathway contribute to delay, and social inequality in delay, may guide interventions and prevention. Literature about this matter is sparse.[26] However, the findings of social inequality in prognostic markers in NHL patients could already be implemented in the clinical practice if GP's and physicians on hospitals paid special attention to patients with low educational level and unspecific symptoms. These subgroups seem to pass more slowly through the diagnostic process. In Denmark a new national Cancer Plan has recently been passed with substantial initiative for awareness and early detection of cancer including cancer with unspecific symptoms. This may have a positive influence on the advancement of NHL at the time of diagnosis and on the social inequality hereof.

Conflict of interest statement

None declared.

Ethical approval

The project did not require approval by the Regional Committee on Biomedical Research Ethics.

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REFERENCES

1. Kogevinas M, Pearce N, Susser M, Boffetta M. *Social inequalities and cancer*. Lyon: International Agency for Research on Cancer; 1997.
2. Menvielle G, Kunst A. Social inequalities in cancer incidence and cancer survival: lessons from Danish studies. *Eur J Cancer* 2008;**44**(14):1933–7.
3. Roswall N, Olsen A, Christensen J, Rugbjerg K, Mellemkjaer L. Social inequality and incidence of and survival from Hodgkin lymphoma, non-Hodgkin lymphoma and leukaemia in a population-based study in Denmark, 1994–2003. *Eur J Cancer* 2008;**44**(14):2058–73.
4. Rachet B, Mitry E, Shah A, Cooper N, Coleman MP. Survival from non-Hodgkin lymphoma in England and Wales up to 2001. *Br J Cancer* 2008;**99**(Suppl. 1):S104–6.
5. Keegan TH, McClure LA, Foran JM, Clarke CA. Improvements in survival after follicular lymphoma by race/ethnicity and socioeconomic status: a population-based study. *J Clin Oncol* 2009;**27**(18):3044–51.
6. Bray C, Morrison DS, McKay P. Socio-economic deprivation and survival of non-Hodgkin lymphoma in Scotland. *Leuk Lymphoma* 2008;**49**(5):917–23.
7. Ewing JC, White JM, Rattray A, Lessells A, Mackie MJ. Total registration of non-Hodgkin's lymphoma and Hodgkin's disease in Scotland: effect of deprivation and caseload on outcome. *Hematology* 2003;**8**(4):211–20.
8. Schwartz KL, Crossley-May H, Vigneau FD, Brown K, Banerjee M. Race, socioeconomic status and stage at diagnosis for five common malignancies. *Cancer Causes Control* 2003;**14**(8):761–6.
9. Brewster DH, Thomson CS, Hole DJ, et al. Relation between socioeconomic status and tumour stage in patients with breast, colorectal, ovarian, and lung cancer: results from four national, population based studies. *BMJ* 2001;**322**(7290):830–1.
10. Mandelblatt J, Andrews H, Kao R, Wallace R, Kerner J. The late-stage diagnosis of colorectal cancer: demographic and socioeconomic factors. *Am J Public Health* 1996;**86**(12):1794–7.
11. Dalton SO, During M, Ross L, et al. The relation between socioeconomic and demographic factors and tumour stage in women diagnosed with breast cancer in Denmark, 1983–1999. *Br J Cancer* 2006;**95**(5):653–9.
12. Frederiksen BL, Osler M, Harling H, Jorgensen T. Social inequalities in stage at diagnosis of rectal but not in colonic cancer: a nationwide study. *Br J Cancer* 2008;**98**(3):668–73.
13. Marengoni A, Winblad B, Karp A, Fratiglioni L. Prevalence of chronic diseases and multimorbidity among the elderly population in Sweden. *Am J Public Health* 2008;**98**(7):1198–200.
14. Oken MM, Creech RH, Tormey DC, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. *Am J Clin Oncol* 1982;**5**(6):649–55.

15. A predictive model for aggressive non-Hodgkin's lymphoma. The International Non-Hodgkin's Lymphoma Prognostic Factors Project. N Engl J Med 1993;329(14):987–94.
16. Wilder RB, Rodriguez MA, Medeiros LJ, et al. International prognostic index-based outcomes for diffuse large B-cell lymphomas. *Cancer* 2002;**94**(12):3083–8.
17. Danish lymphoma group. Year report 2008. Danish lymphoma registry. Danish Lymphoma Group; 2010. Available from: www.lymphoma.dk.
18. Statistics Denmark. IDA – an integrated database for labour market research. Main report; 1991.
19. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987;**40**(5):373–83.
20. Andersen TF, Madsen M, Jorgensen J, Mellemkjoer L, Olsen JH. The Danish National Hospital Register. A valuable source of data for modern health sciences. *Dan Med Bull* 1999;**46**(3):263–8.
21. Galobardes B, Shaw M, Lawlor DA, Lynch JW, Davey SG. Indicators of socioeconomic position (part 2). *J Epidemiol Community Health* 2006;**60**(2):95–101.
22. Turrell G. Income non-reporting: implications for health inequalities research. *J Epidemiol Community Health* 2000;**54**(3):207–14.
23. Hansen RP, Olesen F, Sorensen HT, Sokolowski I, Sondergaard J. Socioeconomic patient characteristics predict delay in cancer diagnosis: a Danish cohort study. *BMC Health Serv Res* 2008;**8**:49.
24. Neal RD, Allgar VL. Sociodemographic factors and delays in the diagnosis of six cancers: analysis of data from the "National Survey of NHS Patients: Cancer". *Br J Cancer* 2005;**92**(11):1971–5.
25. Wamala SP, Murray MA, Horsten M, et al. Socioeconomic status and determinants of hemostatic function in healthy women. *Arterioscler Thromb Vasc Biol* 1999;**19**(3):485–92.
26. Olesen F, Hansen RP, Vedsted P. Delay in diagnosis: the experience in Denmark. *Br J Cancer* 2009;**101**(Suppl. 2):S5–8.