

Acta Oncologica



ISSN: 0284-186X (Print) 1651-226X (Online) Journal homepage: informahealthcare.com/journals/ionc20

Trends in the survival of patients diagnosed with malignant neoplasms of lymphoid, haematopoietic, and related tissue in the Nordic countries 1964–2003 followed up to the end of 2006

Hans H. Storm, Åsa Klint, Laufey Tryggvadóttir, Mette Gislum, Gerda Engholm, Freddie Bray & Timo Hakulinen

To cite this article: Hans H. Storm, Åsa Klint, Laufey Tryggvadóttir, Mette Gislum, Gerda Engholm, Freddie Bray & Timo Hakulinen (2010) Trends in the survival of patients diagnosed with malignant neoplasms of lymphoid, haematopoietic, and related tissue in the Nordic countries 1964–2003 followed up to the end of 2006, Acta Oncologica, 49:5, 694-712, DOI: 10.3109/02841861003631495

To link to this article: <u>https://doi.org/10.3109/02841861003631495</u>



Published online: 21 May 2010.

_	
ſ	
L	D
-	

Submit your article to this journal 🕝

Article views: 1194

\mathbf{O}

View related articles



Citing articles: 14 View citing articles

ORIGINAL ARTICLE

Trends in the survival of patients diagnosed with malignant neoplasms of lymphoid, haematopoietic, and related tissue in the Nordic countries 1964–2003 followed up to the end of 2006

HANS H. STORM¹, ÅSA KLINT², LAUFEY TRYGGVADÓTTIR^{3,4}, METTE GISLUM¹, GERDA ENGHOLM¹, FREDDIE BRAY^{5,6} & TIMO HAKULINEN⁷

¹Department of Cancer Prevention and Documentation, Danish Cancer Society, Strandboulevarden 49, 2100 Copenhagen, Denmark, ²Swedish Cancer Registry, National Board of Health and Welfare, Stockholm, Sweden, ³Icelandic Cancer Registry, Reykjavik, Iceland, ⁴Department of Medicine, University of Iceland, Reykjavik, Iceland, ⁵Department of Clinical- and Registry-based Research, Cancer Registry of Norway, Oslo, Norway, ⁶Department of Biostatistics, Institute of Basic Medical Sciences, University of Oslo, Norway and ⁷Finnish Cancer Registry, Helsinki, Finland

Abstract

Background. Hodgkin lymphoma, Non-Hodgkin lymphoma, multiple myeloma, and acute and other leukaemias constitute about 7% of the overall cancer incidence and 8% of cancer mortality in the Nordic countries. The aim of this study is to describe and interpret the trends in relative survival and excess mortality in the five Nordic populations among these patients. *Material and methods.* Using the NORDCAN database 1964–2003, we estimated age-standardised incidence and mortality rates, 5-year relative survival, and excess mortality rates for varying follow-up periods, and age-specific 5-year relative survival by country, sex, and 5-year diagnostic period. *Results.* Taking into account classification and registration problems in the earlier periods, the patterns of incidence, mortality, and survival are fairly similar between the countries within each cancer form studied. High 5-year relative survival ratios of over 80% were seen in the most recent period 1999–2003 for Hodgkin lymphoma, between 50 and 60% for Non-Hodgkin lymphoma, 38–49% for acute leukaemia and 60–73% for other leukaemia. The variations were between 28 and 41% for multiple myeloma. Danish patients diagnosed with these malignancies tend to fare slightly worse than their Nordic neighbours, with excess mortality rates marginally higher one to three months after diagnosis. *Conclusion.* Although the recent trends and absolute levels of incidence, mortality and survival for the lympho-haematopoietic malignancies are similar, the consistently lower survival of Danish patients – irrespective of type of malignancy – points to an impact of co-morbidity related lifestyle factors, which may negatively affect the chemotherapy and radiation offered as standard treatments for these diseases.

The lymphoid and haematopoietic malignancies constituted 7.4% of the incidence and 8.5% of the mortality in the Nordic countries in 2003 [1]. These neoplasms are rarely localised and have from the beginning of cancer registration activities been subject to classification and coding problems, and hence population-based comparisons have been difficult to conduct at a satisfactory level from both clinical as well as epidemiological perspectives.

Lymphomas have traditionally been grouped into two broad but distinct categories, Hodgkin lymphoma (HL) (0.5% of all cancers) and non-Hodgkin lymphoma (NHL) (3.3%). Some NHL cases may in the past have been misclassified as HL, but with advances in diagnostics, such cases have become increasingly more likely to be correctly classified as NHL. The histological classification of NHL has evolved over many decades, and while over 30 different groupings have been proposed for the study of prognosis and treatment, such categorisations have had limited potential in the study of the aetiological determinants. Risk factors include viral infections, immunodeficiency and immunosuppression, radiation, drugs, and occupational exposure to chemicals, although the aetiology of most NHL remains largely unknown [2,3]. For HL, Epstein Barr virus (EBV) is

(Received 8 December 2009; accepted 14 January 2010)

ISSN 0284-186X print/ISSN 1651-226X online © 2010 Informa UK Ltd. (Informa Healthcare, Taylor & Francis AS) DOI: 10.3109/02841861003631495

Correspondence: Hans H. Storm, Danish Cancer Society, Department of Prevention and Documentation, Strandboulevarden 49, DK 2100 Copenhagen, Denmark. E-mail: hans@cancer.dk



Figure 1. Trends in age-standardised (World) incidence and mortality rates per 100 000 and age-standardised (ICSS) 5-year relative survival for Hodgkin lymphoma by sex and country. Nordic cancer survival study 1964–2003.

a likely cause for some and an association with infectious mononucleosis has been found. The challenge is to determine the causes of the EBV negative tumours where various occupational factors, immune function, and medical conditions including immunodeficiency have been suggested [4]. In EURO-CARE-4, the 5-year age-standardised relative survival of patients with HL was 80% and for NHL 52% [5]. In the period 1958–1987 survival increased in parallel in the Nordic countries for both these malignancies, although the trend in Icelandic HL survival was steeper [6]. The trend in incidence in all Nordic countries up to 1997 was uniformly increasing for NHL but declining somewhat for HL [7]. The Nordic survival was similar or slightly above the European average [5].

Multiple myeloma comprises just below 1.5% of the total cancer incidence, the manifestation of the disease is variable and it can be difficult to diagnose [8]. The suspected risk factors for multiple myeloma include autoimmune disorders, chronic immune stimulation, ionising radiation, occupational exposures, chemicals, alcohol, and tobacco [8]. The incidence varies considerably internationally and detection depends on the availability and use of diagnostic methods. Within the Nordic countries, access to, and utilisation of diagnostic methods are today similar; however, the variable inclusion of MGUS (monoclonal gammopathy of unknown significance), a precursor to multiple myeloma, in the incidence figures may bring about certain differences between countries. Survival was studied in a Nordic study predicting cancer mortality with survival in Denmark about 10 percentage points below the other Nordic countries up to 1987 [6].

Internationally the leukaemias have been classified differently in different studies. The most recent Cancer Incidence in Five Continents Volume has followed the ICD categories for lymphoid, myeloid and unspecified leukaemia, or as one broad category "leukaemia" [9]. In the EUROCARE study, except for "unspecified", the ICD categories were further subdivided into acute and chronic, where the acute is dominated by acute myeloid leukaemia (AML) and the chronic by chronic lymphocytic leukaemia (CLL), however, some countries were unable to present sufficient data [5]. The NORDCAN database as it is today only differentiates between "acute leukaemias", comprising 1% of all cancers, and "other leukaemia" comprising 1.5% [1]. Age is an important factor, given that 20% of all acute leukaemias occur among children (aged 0-14 years at diagnosis), with incidence low up to age 55 and increasing rapidly thereafter. The type that predominates in young age is acute lymphocytic leukaemia (ALL) and is accompanied by acute myeloid leukaemia (AML) among older patients [10]. Other leukaemia is dominated by CLL which, occurs predominantly from ages 55 years and above, and also includes chronic myeloid leukaemia (CML) that in contrast to CLL can be seen in young individuals. Risk factors for leukaemia include both ionising radiation, occupational exposures such as benzene, iatrogenic exposures with radiation and chemotherapy [10].

In this study we follow the survival of Nordic patients diagnosed with HL and NHL, multiple myeloma, and leukaemia, 1964–2003 up until the end of 2006.

Material and methods

We used the NORDCAN database, and hence the data have been checked and converted to well-defined entities, as described by Engholm et al. [11].

We included all cancer patients diagnosed with malignant neoplasms of the lymphoid and haematopoietic tissues (defined as ICD-10 C81-C95) 1964–2003 in Denmark, Finland, Iceland, Norway and Sweden, and supplemented the cancer records with individual records for death up until the end of 2006. The data were analysed according to the individual NORDCAN entities separating the lymphomas into Hodgkin lymphoma (ICD-10 C81) and non-Hodgkin lymphoma (ICD-10 C82-C85, C96), multiple myeloma (ICD-10 C90), and the leukaemias into acute (ICD-10 C91-95 except C9X.0) and other (ICD-10 remaining C91-95). As described in detail [12] we used the cohort survival method for the first seven 5-year periods in each country from 1964–1998, and a hybrid analysis combining period

Table I. Trends in survival for Hodgkin lymphoma by sex and country. Number of tumours (N) included and the 5-year age-standardised (ICSS) relative survival in percent with 95% confidence intervals (RS (CI)). Nordic cancer survival study 1964–2003.

	Γ	enmark	Finland		Ι	celand		Norway	Sweden	
	Ν	RS (CI)	N	RS (CI)	Ν	RS (CI)	N	RS (CI)	N	RS (CI)
Men										
1964-1968	371	36 (31-41)	310	30 (26-36)	15	*	299	34 (28-40)	745	38 (34–43)
1969-1973	410	53 (49-58)	371	49 (44-54)	22	*	313	54 (48-60)	823	51 (47-55)
1974–1978	399	59 (55-64)	323	54 (49-60)	20	*	319	56 (52-62)	677	56 (53-60)
1979–1983	383	64 (59-69)	382	62 (58-67)	14	*	294	65 (61-71)	546	66 (63-70)
1984–1988	388	68 (64-73)	308	71 (67–76)	15	*	238	70 (65–75)	551	71 (68–75)
1989–1993	394	75 (70-80)	330	71 (67–75)	18	*	268	76 (71-81)	487	78 (75–82)
1994–1998	359	75 (71–79)	374	80 (76-85)	19	*	264	82 (78-87)	490	80 (77-83)
1999–2003	357	80 (77-84)	362	85 (81-88)	29	*	315	84 (81-88)	454	84 (81-86)
Women										
1964-1968	249	45 (40-51)	226	44 (39–51)	7	*	227	50 (43-57)	507	47 (42-52)
1969–1973	298	56 (51-62)	235	54 (48-60)	12	*	210	61 (55-68)	511	57 (52-62)
1974–1978	247	63 (58–69)	254	66 (61-71)	11	*	215	65 (60-70)	455	63 (59–68)
1979–1983	258	69 (64-75)	252	70 (65–76)	7	*	199	70 (65–75)	415	70 (66–74)
1984–1988	219	72 (66–77)	262	73 (68–78)	4	*	170	75 (69-81)	397	75 (71–79)
1989–1993	246	73 (68–79)	261	80 (76-86)	8	*	165	78 (72-85)	386	78 (74-82)
1994–1998	241	79 (74–85)	284	83 (79-87)	10	*	180	85 (79–91)	362	82 (79-86)
1999–2003	261	84 (81-88)	291	84 (81-88)	15	*	232	85 (82-89)	405	84 (81-87)

*Too few patients to calculate survival, see ref. [12].



Figure 2. Trends in age-standardised (ICSS) excess death rates per 100 person years for Hodgkin lymphoma by sex, country, and time since diagnosis in Nordic cancer survival study 1964–2003. No Icelandic curves. Too few patients to calculate rates for Iceland.

and cohort survival in the last period 1999-2003 [13]. Country-specific life tables were used to calculate the expected survival. Age-standardisation was performed using standard weight distributions (ICSS standards) as in the EUROCARE-4 analysis [14]. Patients were followed until death, emigration or loss to follow-up or to the end of 2006. Excess mortality rates were stratified into short intervals after the diagnosis: the first month, one to three months, 4-12 months and yearly intervals thereafter. We present age-standardised (World) incidence and mortality rates, 5-year relative survival ratios and excess mortality rates for the follow-up periods, the first month, one to three months and two to five years following diagnosis, as well as age-specific 5-year relative survival ratios by country, sex and age.

Results

Hodgkin lymphoma (C81)

Incidence and mortality. Hodgkin lymphoma is a rare malignancy with an age-standardised incidence of 2 to 3 per 100 000 for both men and women in

the Nordic countries. For males, incidence slowly decreased since 1970 when it peaked at around 3 per 100 000 (Figure 1). There was a corresponding decreasing trend among women until the early-1980s. Incidence rose again thereafter and ended in 1999–2003 at about the same level observed in the mid-1960s. In recent years, incidence has been lowest in Sweden in both sexes and highest in Finland (and Iceland, although based on small numbers). Mortality rates constantly decreased during the period of observation (Figure 1). Compared to females, the mortality levels in men were slightly higher in all countries, about 0.3 per 100 000 among men and 0.2 among women.

Survival. Age-standardised 5-year relative survival has increased in a similar manner in all Nordic countries and is currently about 85% for both sexes, except for males in Denmark where it is slightly lower (Figure 1, Table I). Evaluating survival in terms of excess mortality as a function of time since diagnosis reveals some differences. Excess mortality during the first month after diagnosis was more uneven between countries among women in the early years and was reduced to about 50 per 100 person

698 H. H. Storm et al.

Table II. Trends in 5-year age-specific relative survival in percent after Hodgkin lymphoma by sex and country. Nordic cancer survival study 1964-2003.

			Me	n		Women						
Age	0–29	30–39	40-49	50–69	70–89	90+	0–29	30–39	40-49	50–69	70–89	90+
Denmark												
1964-1968	54	41	37	24	5	*	72	51	44	23	8	*
1969-1973	75	73	46	30	18	*	82	63	46	43	20	*
1974–1978	79	77	61	40	16	*	80	94	70	40	13	*
1979–1983	75	76	71	56	26	*	89	71	97	51	28	*
1984–1988	87	83	79	57	15	*	91	88	79	57	21	*
1989-1993	91	84	77	64	40	*	85	86	94	60	31	*
1994–1998	92	90	91	69	12	*	90	94	86	62	49	*
1999–2003	95	94	90	73	34	*	94	94	91	83	48	*
Finland												
1964-1968	47	35	32	18	7	*	69	65	31	17	14	*
1969-1973	73	54	52	35	9	*	80	60	76	28	7	*
1974–1978	75	66	61	32	21	*	86	86	65	39	31	*
1979–1983	87	72	59	42	25	*	91	88	62	59	26	*
1984–1988	94	82	70	64	18	*	91	88	77	59	30	*
1989–1993	88	90	81	62	10	*	97	94	87	63	45	*
1994-1998	91	88	95	76	41	*	96	95	98	73	39	*
1999–2003	94	92	96	78	53	*	97	97	99	71	46	*
Iceland												
1964–1968	62	*	*	12	*	*	*	*	*	*	*	*
1969–1973	62	*	*	12	*	*	*	*	*	*	*	*
1974-1978	92	*	*	*	*	*	*	*	*	*	*	*
1979–1983	92	*	*	*	*	*	*	*	*	*	*	*
1984–1988	89	*	*	105	*	*	*	*	*	*	*	*
1989–1993	89	*	*	105	*	*	*	*	*	*	*	*
1994–1998	97	100	101	86	*	*	*	*	*	*	*	*
1999-2003	97	100	101	86	*	*	*	*	*	*	*	*
Norway												
1964–1968	41	48	37	27	4	*	71	72	51	22	10	*
1969–1973	75	55	55	40	27	*	83	78	73	34	17	*
1974–1978	84	76	53	31	8	*	86	87	91	31	12	*
1979–1983	83	89	68	48	16	*	89	97	76	51	14	*
1984–1988	99	78	77	47	21	*	92	85	91	68	20	*
1989–1993	92	82	84	74	27	*	91	90	93	67	40	*
1994–1998	93	93	96	86	28	*	94	98	94	81	44	*
1999–2003	97	95	93	83	37	*	95	97	93	88	38	51
Sweden												
1964–1968	56	47	39	22	10	*	70	62	39	26	11	*
1969–1973	78	63	41	32	12	*	84	72	51	32	18	0
1974–1978	80	70	61	35	13	*	87	73	70	42	23	*
1979–1983	86	82	71	43	32	*	87	89	78	50	25	*
1984–1988	94	88	83	44	26	*	95	93	67	62	32	*
1989–1993	93	90	87	72	30	*	93	92	84	69	33	52
1994-1998	95	95	93	65	37	*	96	93	101	73	33	*
1999–2003	94	98	94	76	43	*	96	93	99	76	45	*

Numbers in *italics* indicate that two or more cells had to be combined to get sufficient number of patients to calculate survival. ^{*}Too few patients to calculate survival, see ref. [12].

years by the early-1980s (Figure 2). Finnish women had a low excess mortality from the 1960s. The reduction of excess death rates among males soon after diagnosis has taken place more gradually, but the excess death rates are currently at about the same level as among women. The excess death rates one to three months after diagnoses have dropped in Norway and Sweden for both sexes and among males in Finland, and to some extent among males in Denmark. No substantial changes with calendar time were seen for Danish and Finnish women one to three months after diagnosis, but within two to five years of follow-up there were few differences between the countries. Iceland was not included in the comparisons as the number of cases was small.

Survival declined with increasing age in all countries. In patients aged 70–89, the 5-year relative



Figure 3. Trends in age-standardised (World) incidence and mortality rates per 100 000 and age-standardised (ICSS) 5-year relative survival for non-Hodgkin lymphoma by sex and country. Nordic cancer survival study 1964–2003.

survival was below or close to 50% although there were considerable differences between the countries, especially in males (survival in Denmark was 34, Norway 37, Sweden 43, and Finland 53%). Survival has increased over the years in all age groups, most notably in 40–49-year-olds, where relative survival was around 40–50% in the 1960s, but rose to above 90% in all countries in the latest study period (Table II).

Non-Hodgkin lymphoma (C82-C85,C96)

Incidence and mortality. The incidence increased in all the Nordic countries (Figure 3) until the 1990s,

and in 2003 the age-standardised incidence among men varied between 10 per 100 000 in Sweden to 12.2 in Denmark and for women between 7.1 (Sweden) to 8.8 (Denmark). Mortality has also increased but to a lesser extent than incidence, with a slight decline after year 2000 (Figure 3). Over the years, but notably from the late-1980s, the gap between incidence and mortality has widened.

Survival. The 5-year age-standardised relative survival increased from around 20–30% in 1964–1968 to 50–60% in 1999–2003 and was marginally higher in women than in men (Figure 3; Table III). The

	Γ	Denmark		Finland		Iceland	N	Jorway	Sweden		
	N	RS (CI)	N	RS (CI)	N	RS (CI)	Ν	RS (CI)	Ν	RS (CI)	
Men											
1964-1968	664	24 (20-29)	553	24 (18-33)	16	29 (16–53)	568	23 (19-28)	1 166	23 (20-26)	
1969-1973	836	20 (17-23)	630	24 (19-29)	21	29 (16-53)	589	27 (23-32)	1 431	28 (25-31)	
1974–1978	979	28 (24-31)	789	29 (25-34)	24	52 (28-97)	783	36 (32-40)	1 512	32 (29-35)	
1979-1983	1 191	34 (31–38)	997	37 (32-41)	28	46 (27-77)	893	40 (36-44)	1 633	41 (38–44)	
1984–1988	1 447	38 (35-42)	1 229	38 (35–42)	48	30 (21-44)	1 216	44 (41-48)	2 308	47 (44-49)	
1989-1993	1 724	43 (40-46)	1 659	42 (39-45)	67	42 (30-58)	1 445	43 (40-46)	3 188	49 (47-51)	
1994–1998	1 914	43 (41-46)	2 013	47 (45-50)	93	51 (40-66)	1 677	47 (44-50)	3 380	50 (48-52)	
1999-2003	2 014	50 (48-53)	2 260	53 (51-55)	101	56 (47-67)	1 748	51 (48-53)	3 703	54 (53-56)	
Women											
1964-1968	565	25 (21-28)	425	20 (16-25)	8	20 (10–39)	462	28 (24-34)	903	28 (25-31)	
1969-1973	681	26 (22-30)	509	29 (25-35)	12	20 (10-39)	509	31 (27-35)	1 154	33 (30–36)	
1974–1978	805	32 (28-35)	718	35 (32-40)	20	45 (31–65)	631	39 (35–43)	1 163	39 (36-42)	
1979-1983	997	40 (37-43)	1 022	40 (37-44)	27	45 (31–65)	810	49 (45-53)	1 211	43 (40-46)	
1984–1988	1 325	45 (42-48)	1 375	44 (41-47)	26	54 (32-88)	1 086	50 (47-54)	1 912	49 (47–52)	
1989–1993	1 566	50 (47-53)	1 774	49 (46-51)	40	60 (45-81)	1 303	54 (51-57)	2 565	54 (52-56)	
1994–1998	1 681	52 (50-55)	2 078	51 (49-54)	66	54 (43-68)	1 437	52 (50-55)	2 925	57 (55-59)	
1999–2003	1 797	55 (53–57)	2 234	58 (56-60)	74	57 (48-68)	1 643	57 (55-59)	3 111	60 (58–61)	

Table III. Trends in survival for non-Hodgkin lymphoma by sex and country. Number of tumours (N) included and the 5-year agestandardised (ICSS) relative survival in percent with 95% confidence intervals (RS (CI)). Nordic cancer survival study 1964–2003.

Numbers in *italics* indicate that two or more cells had to be combined to get sufficient number of patients to calculate survival.

differences between the Nordic countries were small in general, however, with survival highest in Sweden and lowest in Finland and Denmark. Age at diagnosis is an important predictor of the 5-year relative survival in all calendar periods, highest (between 70–80%) for cancers diagnosed in 1999–2003 at ages 0–49 years and falling to 40–50% for ages 70–79. The survival estimates were fairly similar across the Nordic countries (Table IV).

The excess death rates by calendar period and time since diagnosis (Figure 4) clearly demonstrate that the inter-country differences, especially in earlier time periods, were largest during the first month of follow-up and largely were eliminated after two years of follow-up. The differences in excess death rates between the Nordic countries have diminished by calendar time and were minor from the late 1980s onwards.

Multiple myeloma (C90)

Incidence and mortality. The incidence increased among men in the Nordic countries reaching a stable rate of 3 per 100 000 in the mid-1980s, except for Norway where the incidence reached 4.3 (Figure 5). For women, the incidence followed the same pattern and reached a level of 2 to 3 per 100 000 for the period 1999–2003. The mortality rate followed the incidence at a slightly lower level, reaching 2–3 per 100 000 among men and about 1.5 in women while decreasing slightly from the late-1980s (Figure 5). Survival. The 5-year age-standardised relative survival was similar for men and women (Table V) and among males increased steadily over the observation period in each country from below 20 to 28% in Denmark, to 29% in Iceland, and to 34, 36, and 37% in Finland, Norway and Sweden, respectively by 1999-2003. In women, the most recent survival estimates ranged from between 29 and 41%. The excess mortality was highest during the first month after diagnosis and in Denmark, although for the most recent time period, the rate of Finland ranked first (Figure 6). The difference between countries largely disappeared with calendar time, as did the level of the excess mortality during the first month, diminishing to one third of that seen in 1964-1968. The excess death rates in the period one to three months after diagnosis were almost the same in all countries and decreased slightly over time. Two to five years after diagnosis the excess death rates were lower and similar over time and between countries. The survival also depended on age at diagnosis (Table VI), with patients diagnosed at younger ages having higher levels of survival than patients diagnosed at older ages. It is noteworthy that, relative to the other countries, Danish patients diagnosed at ages 0-49 in the period 1999-2003 had a rather low survival - between 15-26 percentage points lower in men and 14-19 percentage points lower in women. Sweden and Norway had the highest survival in almost all age groups for patients diagnosed 1999-2003.

			Μ	len		Women						
Age	0–49	50–59	60–69	70–79	80–89	90+	0–49	50–59	60–69	70–79	80-89	90+
Denmark												
1964-1968	34	31	29	16	15	0	37	37	32	18	0	0
1969-1973	27	26	24	15	8	0	37	35	25	22	15	0
1974-1978	41	35	30	25	10	0	50	43	36	22	14	0
1979–1983	53	50	38	26	12	0	59	59	45	29	15	37
1984–1988	57	50	37	32	24	50	75	61	49	33	20	29
1989-1993	61	55	49	35	21	31	74	63	54	38	28	24
1994-1998	60	58	46	38	20	0	77	66	58	42	27	13
1999-2003	69	64	55	41	31	0	78	73	61	44	28	13
Finland												
1964-1968	28	25	21	11	51	*	33	29	21	13	9	*
1969-1973	43	25	30	16	10	*	39	43	25	25	21	*
1974–1978	49	40	27	29	7	*	56	41	41	28	18	0
1979–1983	53	43	33	33	29	0	63	52	44	30	21	*
1984–1988	63	50	41	30	16	0	68	61	47	34	19	30
1989–1993	71	56	45	30	18	0	75	64	53	36	26	26
1994–1998	75	57	49	40	25	0	79	71	55	39	23	18
1999-2003	77	67	57	42	31	3	83	75	63	48	27	14
Iceland												
1964-1968	46	46	24	20	20	*	51	51	18	*	*	*
1969-1973	46	46	24	20	20	*	51	51	18	*	*	*
1974–1978	46	46	51	58	58	*	71	71	41	30	30	*
1979–1983	58	58	*	66	66	*	71	71	41	30	30	*
1984–1988	70	70	37	0	0	*	59	59	43	56	56	*
1989–1993	56	56	55	25	25	*	62	62	70	52	52	*
1994–1998	56	56	52	48	48	*	91	91	31	44	44	*
1999–2003	78	78	58	40	40	*	91	91	47	41	41	*
Norway												
1964–1968	39	40	17	19	11	0	48	37	33	19	14	*
1969–1973	46	38	30	12	23	*	49	46	34	23	8	*
1974–1978	53	49	36	28	20	*	49	49	50	30	16	0
1979–1983	57	51	39	33	28	*	63	62	49	39	41	0
1984-1988	60	52	47	36	35	0	62	74	47	43	34	0
1989-1993	63	64	41	36	19	0	73	62	63	46	28	72
1994–1998	65	61	51	41	23	53	71	69	55	46	27	22
1999–2003	75	68	53	43	23	23	80	68	64	50	28	24
Sweden												
1964–1968	34	30	23	19	16	81	41	35	32	22	12	0
1969-1973	43	42	25	20	23	0	46	40	35	28	21	0
1974–1978	49	43	34	26	14	120	56	52	43	30	22	26
1979–1983	65	53	42	34	20	0	69	59	45	33	17	0
1984–1988	72	61	47	35	32	0	71	63	49	43	29	21
1989–1993	68	59	51	43	29	15	76	69	57	46	29	0
1994–1998	75	63	52	42	28	15	80	72	61	49	28	18
1999-2003	77	68	57	46	33	46	82	78	63	49	35	20

Table IV. Trends in 5-year age-specific relative survival in percent after non-Hodgkin lymphoma by sex and country. Nordic cancer survival study 1964–2003.

Numbers in *italics* indicate that two or more cells had to be combined to get sufficient number of patients to calculate survival. *Too few patients to calculate survival, see ref. [12].

Acute and other leukaemia (C91–95)

Incidence and mortality. The trends in incidence for both acute and other leukaemia were fairly similar in all countries, except Sweden, with rates for acute leukaemia slightly increasing until the mid-1980s to a level of 4 to 5 in men, and between 3 and 4 per 100 000 in women (Figure 7). The incidence of acute and other leukaemia in Sweden was low compared to the

other Nordic countries until the late-1980s, although corresponding mortality was similar across the Nordic populations. The incidence of other leukaemia was a little higher for men ranging between 4 and 6 but somewhat lower for women at between 2 and 3 per 100 000 (Figure 8). The mortality from both acute and other leukaemia has declined over time, particularly for the latter group. For both cancer



Figure 4. Trends in age-standardised (ICSS) excess death rates per 100 person years for non-Hodgkin lymphoma by sex, country, and time since diagnosis in Nordic cancer survival study 1964–2003.

forms the mortality levels in the last period have been close to 2 per 100 000 (Figures 7 and 8).

Survival and excess mortality. In agreement with the above trends, 5-year age-standardised relative survival for acute leukaemia increased during the observation period from below 10 to above 40% for both sexes (Table VII), as that did for other leukaemia, from below or close to 20% to a level of between 60-70% in the last study period, with little difference observed between the Nordic countries (Table VIII). It is noteworthy that the survival increases were seen at ages of diagnosis up to 70 years (Table IX), with survival estimates between 72-81% in men and women diagnosed below the age of 50 in Denmark, Finland, Norway and Sweden in 1999-2003. For other leukaemia, a similar pattern emerged (Table X) and here quite large increases in survival in the older age groups were observed.

The excess mortality rates for both leukaemia groups (Figures 9 and 10) were highest in the earliest time periods and also within the first month of diagnosis, with a clear decline in excess mortality by calendar year of diagnosis. There were no substantial differences between the countries, and the excess mortality rates one to three months after diagnosis were lower than in the first month, with only minor differences between the countries and over time two to five years after diagnosis.

Discussion

Large randomised international trials and advances in diagnostics and staging procedures have resulted in major improvements in chemotherapeutic regimes with fewer side effects and better average outcomes among patients diagnosed with cancers of the lymphatic and haematopoietic tissues. While individuallytailored treatments may have a more important role in the future, conventional chemotherapy remains the effective and standard mode of treatment at present. HL is an early example of the benefits of large randomised trials, leading to clear improvements in both radiotherapy and chemotherapy, and with treatment for childhood leukaemia paving the way for more effective therapies for other lymphomas and leukaemias. The use of cytotoxic drugs moving from single agents decades ago to combination regimes, coupled



Figure 5. Trends in age-standardised (World) incidence and mortality rates per 100 000 and age-standardised (ICSS) 5-year relative survival for multiple myeloma by sex and country. Nordic cancer survival study 1964–2003.

with an increasing ability to reduce the impact of side effects and thereby increasing drug tolerance, are clearly reflected in the increasing relative survival and declining mortality over time, contrasting the relatively stable incidence. The EUROCARE-4 study [5] points to survival in Eastern Europe being lower than in other areas, perhaps further supporting the importance of the adoption of new technologies for better diagnostics and financial capabilities to afford new drugs in the treatment of these patients. The reduction of excess mortality during the first months after diagnosis over time also indicates that there is a tendency toward initiating treatment immediately, although clearly there are still some variations in this practice.

Patients in Denmark have a higher excess mortality one to three months after diagnosis than their Nordic counterparts, which may indicate later diagnoses leading to less favourable effects of treatment, or co-morbidity resulting in death from competing causes. Supportive care during the first months after diagnosis also plays a role in patient survival, but we have no reason to suspect that the quality differs materially between the Nordic countries. A minor part of the earlier increases in HL survival might be

]	Denmark		Finland		Iceland		Norway	Sweden		
	N	RS (CI)	N	RS (CI)	N	RS (CI)	N	RS (CI)	N	RS (CI)	
Men											
1964-1968	376	16 (12-20)	245	15 (10-22)	8	*	420	18 (14-23)	516	19 (15-23)	
1969-1973	438	13 (10-17)	308	20 (16-25)	8	*	511	25 (21-30)	699	22 (19-26)	
1974–1978	493	15 (12–19)	385	32 (26-38)	22	41 (27–60)	674	30 (26-34)	817	29 (25-33)	
1979–1983	597	17 (14–21)	435	32 (27–38)	34	41 (27–60)	743	28 (25–32)	1 081	31 (28–34)	
1984–1988	625	22 (18-26)	594	33 (29–38)	33	31 (20-49)	742	30 (26-34)	1 331	32 (29-35)	
1989-1993	664	21 (18-25)	570	28 (24-32)	25	31 (20-49)	707	33 (29-37)	1 437	32 (30-35)	
1994–1998	703	23 (20-27)	593	31 (27-35)	36	29 (19–42)	797	33 (30–37)	1 443	36 (33–39)	
1999–2003	759	28 (25-31)	663	34 (31-37)	25	29 (19–42)	798	36 (33–39)	1 475	37 (35–39)	
Women											
1964-1968	296	14 (10-19)	255	14 (10-21)	5	*	382	17 (13-22)	392	18 (14-23)	
1969-1973	355	14 (10-18)	413	23 (18-29)	9	*	429	25 (20-31)	611	23 (19-27)	
1974–1978	415	20 (16-25)	453	29 (25-34)	14	19 (9–39)	584	29 (25-34)	721	33 (29-37)	
1979–1983	522	16 (13-21)	632	33 (29–38)	24	19 (9–39)	615	35 (31-40)	953	32 (29-36)	
1984–1988	577	23 (19-27)	703	35 (31-40)	32	47 (34–65)	645	28 (24-33)	1 116	35 (32-39)	
1989-1993	616	25 (22-30)	649	30 (26-34)	25	47 (34–65)	633	31 (27–36)	1 160	35 (32–38)	
1994–1998	589	29 (25-33)	824	32 (29-36)	32	30 (17-54)	642	35 (31-40)	1 218	37 (34-40)	
1999–2003	623	33 (30–36)	703	33 (31–36)	30	29 (18-48)	758	38 (35-42)	1 300	41 (38–43)	

Table V. Trends in survival for multiple myeloma by sex and country. Number of tumours (N) included and the 5-year age-standardised (ICSS) relative survival in percent with 95% confidence intervals (RS (CI)). Nordic cancer survival study 1964–2003.

Numbers in *italics* indicate that two or more cells had to be combined to get sufficient number of patients to calculate survival. *Too few patients to calculate survival, see ref. [12].

attributed to artefact in that certain NHL cases associated with poorer prognosis may have been previously misclassified as HL, but with advances in diagnostics, such cases have become increasingly more likely to be correctly classified as NHL [15].



Figure 6. Trends in age-standardised (ICSS) excess death rates per 100 person years for multiple myeloma by sex, country, and time since diagnosis in Nordic cancer survival study 1964–2003.

			Me	en		Women						
Age	0-49	50–59	60–69	70–79	80–89	90+	0–49	50–59	60–69	70–79	80–89	90+
Denmark												
1964-1968	29	24	18	6	9	*	6	25	18	11	5	*
1969-1973	24	12	13	12	4	0	28	25	15	4	4	*
1974-1978	12	21	18	11	13	*	36	33	24	13	0	*
1979-1983	29	27	16	13	8	*	34	24	16	10	8	*
1984-1988	36	29	19	17	15	*	41	38	20	16	9	*
1989-1993	32	27	20	16	17	0	33	31	25	26	15	0
1994-1998	49	43	23	11	6	*	58	41	28	20	11	0
1999-2003	46	47	29	17	8	0	59	49	36	21	10	0
Finland												
1964-1968	24	11	19	17	0	*	22	25	11	9	11	*
1969-1973	39	36	21	11	0	*	24	25	24	20	24	*
1974-1978	51	43	33	22	20	*	51	27	37	25	7	*
1979-1983	42	40	46	18	17	0	59	43	36	25	12	0
1984-1988	51	49	35	24	13	0	61	39	40	25	19	0
1989-1993	62	41	26	19	5	0	52	46	35	17	6	0
1994-1998	60	59	31	13	9	0	65	48	33	23	6	0
1999-2003	68	62	35	17	8	0	78	47	35	20	5	8
Iceland												
1964-1968	31	31	31	*	*	*	24	24	24	*	*	*
1969-1973	31	31	31	*	*	*	24	24	24	*	*	*
1974-1978	33	33	33	50	52	*	19	19	19	10	34	*
1979-1983	33	33	33	50	52	*	19	19	19	10	34	*
1984-1988	39	39	39	18	29	*	49	49	49	43	51	*
1989-1993	39	39	39	18	29	*	49	49	49	43	51	*
1994-1998	37	37	37	20	12	*	39	39	39	29	*	*
1999-2003	37	37	37	20	12	*	25	25	25	38	29	*
Norway												
1964–1968	26	21	18	14	14	*	28	21	20	12	9	*
1969-1973	47	24	25	22	14	*	36	28	27	18	22	0
1974–1978	62	32	28	23	17	0	53	38	31	20	16	0
1979-1983	64	30	30	22	8	0	43	58	33	29	18	0
1984-1988	49	36	30	27	12	0	28	34	28	35	10	0
1989-1993	60	44	34	21	17	0	45	46	27	28	19	0
1994-1998	58	51	37	22	9	0	58	43	35	28	23	0
1999-2003	61	56	40	23	14	60	73	56	36	28	15	1
Sweden												
1964-1968	33	30	22	11	4	*	28	26	19	9	14	*
1969-1973	37	31	23	17	11	0	39	34	23	16	8	*
1974-1978	50	29	34	23	13	*	64	37	35	24	16	0
1979–1983	55	41	29	26	9	69	55	35	34	26	18	0
1984–1988	49	36	35	27	17	0	52	44	38	29	18	0
1989-1993	51	46	35	24	12	0	46	52	36	29	16	0
1994-1998	62	54	36	25	14	52	58	62	37	25	17	0
1999–2003	72	54	37	25	12	1	73	61	40	27	18	18

Table VI. Trends in 5-year age-specific relative survival in percent after multiple myeloma by sex and country. Nordic cancer survival study 1964–2003.

Numbers in *italics* indicate that two or more cells had to be combined to get sufficient number of patients to calculate survival. *Too few patients to calculate survival, see ref. [12].

The survival of NHL patients is rather homogenous in the Nordic populations and close to, or above the European average [5], although substantially lower (30 percentage points) than the survival observed among HL patients. The lack of variation is in contrast to the European picture of heterogeneity and a clear east-west gradient, with the poorest survival seen in several Eastern European populations [5]. The interpretation of the definition of NHL and the treatment options likely differ by European region, but it is probable that definitions and the quality of treatment and care within the Nordic countries are fairly similar, especially after the formation of the Nordic Lymphoma Group (*www.nordic-lymphoma.org*). The only differences we have seen are an overrepresentation of elderly patients with NHL in Sweden and a somewhat younger distribution of patients in Iceland [1], although neither appears to



Figure 7. Trends in age-standardised (World) incidence and mortality rates per 100 000 and age-standardised (ICSS) 5-year relative survival for acute leukaemia by sex and country. Nordic cancer survival study 1964–2003.

have impacted on the age-standardised survival rates. Also during the study period, we observed the effect of changes in classification, most notably in Sweden, leading to an incidence level in 2003 not dissimilar to 1989. This is likely a consequence of new coding rules separating more precisely chronic lymphocytic leukaemias and lymphomas. That there has been a slight downturn in mortality in the last decade, coupled with a steady increase in relative survival to a level similar across countries, points to the likelihood of concurrent adoption of new therapies as a result of international collaborations in haematology such as the CALGB (Cancer and Leukaemia Group B) initiated in the USA in the mid-1950s, and in the Nordic countries the national and the Nordic Lymphoma Group established from the 1980s. The observed pattern of a high excess rate of deaths during the first three months after diagnosis from the 1960s to the 1980s and a levelling off thereafter are also indicative of an effect of the improvement of chemotherapy and radiotherapy and a widespread use of these treatment modalities.

Assuming that the incidence of multiple myeloma is defined in the same way in all of the

	Denmark		Finland			Iceland		Norway	Sweden	
	Ν	RS (CI)	Ν	RS (CI)	Ν	RS (CI)	Ν	RS (CI)	Ν	RS (CI)
Men										
1964-1968	429	3 (1-5)	377	2 (1-4)	19	*	457	1 (1-4)	404	7 (5-12)
1969-1973	594	8 (5–11)	387	3 (2-5)	24	*	479	7 (5–10)	581	9 (6-13)
1974–1978	606	14 (11-18)	445	9 (7-12)	20	*	501	17 (13-21)	623	14 (11-18)
1979–1983	713	17 (14–20)	506	19 (15-23)	34	*	545	20 (17-25)	806	17 (15-20)
1984–1988	736	28 (24-32)	526	30 (26-34)	24	*	533	30 (25-36)	960	31 (28-35)
1989–1993	752	31 (27-35)	498	37 (32-42)	30	*	442	36 (31-42)	997	33 (30-37)
1994–1998	669	35 (31-40)	563	39 (35-44)	35	*	442	34 (29-40)	970	41 (37-45)
1999–2003	809	41 (38–45)	586	42 (38-46)	28	*	487	38 (33-43)	1 018	43 (40-46)
Women				. ,						
1964-1968	337	1 (0-3)	378	3 (1-6)	14	*	353	3 (1-6)	318	8 (5–13)
1969-1973	488	6 (4-9)	361	6 (4-10)	18	*	390	9 (6-12)	466	12 (8-16)
1974–1978	551	15 (12–19)	433	14 (11–18)	20	10 (4-22)	470	13 (10-17)	582	18 (15-22)
1979–1983	623	21 (17-25)	513	24 (20-28)	21	10 (4-22)	441	21 (17-25)	771	25 (21-28)
1984–1988	676	27 (24–32)	522	31 (26–35)	32	51 (38–68)	434	28 (23-34)	881	29 (26-32)
1989–1993	596	29 (25-33)	527	42 (37-47)	26	51 (38–68)	383	33 (28–39)	866	36 (32-39)
1994–1998	666	36 (31-41)	568	47 (42–52)	26	40 (30–53)	431	42 (37-47)	964	41 (38–45)
1999–2003	674	42 (38–46)	610	49 (45–53)	30	40 (30–53)	417	44 (40–50)	922	46 (43-49)

Table VII. Trends in survival for acute leukaemia by sex and country. Number of tumours (N) included and the 5-year age-standardised (ICSS) relative survival in percent with 95% confidence intervals (RS (CI)). Nordic cancer survival study 1964–2003.

Numbers in *italics* indicate that two or more cells had to be combined to get sufficient number of patients to calculate survival. *Too few patients to calculate survival, see ref. [12].

Nordic countries, it is of note that survival appears to differ between the Nordic countries. Only in Sweden, Finland and Norway has survival reached the reported European average in EUROCARE-4 [5], although it is apparent that the definition of multiple myeloma and diagnostics varies across Europe. The excess mortality during the first month after diagnosis and the somewhat poorer survival among younger patients in Denmark may reflect Denmark's position as the country with the poorest survival among the Nordic countries. Since treatment is considered to be similar in the Nordic countries [16,17], and a Nordic collaboration (NMSG – Nordic Myelomatosis Study Group) dedicated to multiple myeloma and MGUS has been studying differences in incidence and survival without any clear cut explanations as yet,

Table VIII. Trends in survival for other leukaemia by sex and country. Number of tumours (N) included and the 5-year age-standardised (ICSS) relative survival in percent with 95% confidence intervals (RS (CI)). Nordic cancer survival study 1964–2003.

	Denmark			Finland		Iceland		Norway	Sweden		
	N	RS (CI)	N	RS (CI)	Ν	RS (CI)	N	RS (CI)	N	RS (CI)	
Men											
1964-1968	752	18 (15-21)	479	25 (20-31)	9	14 (5–44)	465	18 (15-23)	834	18 (15-22)	
1969-1973	765	24 (20-28)	580	25 (21-29)	16	14 (5–44)	535	21 (17-25)	1 029	22 (19-25)	
1974–1978	898	25 (22-29)	587	37 (33-42)	28	32 (20–52)	584	30 (26-35)	1 191	30 (27-33)	
1979–1983	1 028	33 (30–37)	659	43 (38–48)	23	32 (20-52)	598	36 (32-41)	1 525	38 (36-41)	
1984–1988	1 1 3 4	41 (38-45)	731	45 (41-50)	39	55 (38-80)	565	38 (33–43)	1 598	46 (43-49)	
1989-1993	1 089	49 (46-53)	649	52 (47-56)	28	64 (46-88)	659	46 (42-51)	1 489	54 (51-57)	
1994-1998	1 220	56 (53-60)	708	54 (50-58)	37	66 (49-90)	787	53 (49-57)	1 780	62 (59-65)	
1999-2003	1 278	63 (60-65)	746	55 (52–58)	45	71 (59-85)	929	58 (55-61)	1 886	68 (66-70)	
Women											
1964-1968	433	25 (21-30)	444	25 (21-30)	10	18 (7–46)	376	21 (17-26)	544	19 (16-24)	
1969-1973	468	30 (26-35)	502	36 (31-42)	14	18 (7–46)	337	30 (25-37)	694	25 (22-29)	
1974–1978	601	31 (27-36)	520	42 (38-47)	13	42 (25–71)	377	36 (31-42)	770	38 (34-42)	
1979–1983	689	43 (39–48)	616	49 (45-54)	12	42 (25–71)	424	39 (34-45)	989	41 (37-44)	
1984–1988	735	47 (43–52)	603	53 (49–58)	18	52 (39–70)	417	39 (34–45)	986	50 (47-54)	
1989–1993	829	57 (53-61)	546	53 (48-58)	27	52 (39–70)	500	53 (48-58)	987	59 (56-63)	
1994–1998	870	63 (59-67)	600	54 (49-59)	29	59 (42-83)	615	62 (57-67)	1 1 2 5	66 (63–69)	
1999–2003	915	68 (65–71)	558	60 (56–64)	28	68 (54-86)	662	64 (61–68)	1 244	70 (68–73)	

Numbers in *italics* indicate that two or more cells had to be combined to get sufficient number of patients to calculate survival.



Figure 8. Trends in age-standardised (World) incidence and mortality rates per 100 000 and age-standardised (ICSS) 5-year relative survival for other leukaemia by sex and country. Nordic cancer survival study 1964–2003.

co-morbidity could be a candidate as an explanatory factor.

The Nordic countries are rather similar with respect to rates of leukaemia incidence, as are trends in incidence, mortality and survival for both acute and other leukaemias. The only exception is Sweden where the underreporting of leukaemia and lymphoma incidence is evident until the 1980s [18] and still present in 1998 [19], and clearly indicated by the higher mortality than incidence rates during this period. The reason for the underreporting is largely unknown but may be due to the fact that leukaemias are often diagnosed at haematology departments without the use of services from pathology departments. Reporting from pathology labs are traditionally well integrated with cancer registration however reported to be less so in Sweden [19]. The problems in reporting is to some extent counteracted in the other Nordic countries by supplementary use of information from death certificates which is not the case in Sweden. It is worthy of note that survival after an acute leukaemia is similar in each Nordic population, even in the period where registration is considered incomplete in Sweden. We see the same

			Μ	len		Women						
Age	0–29	30–49	50–69	70–79	80-89	90+	0–29	30–49	50–69	70–79	80-89	90+
Denmark												
1964-1968	4	3	1	0	0	*	2	0	0	3	0	*
1969-1973	14	7	3	4	0	*	17	2	1	0	0	*
1974–1978	24	17	3	2	0	*	37	6	8	2	0	*
1979–1983	38	12	4	1	0	0	45	17	5	3	0	0
1984–1988	53	28	8	1	0	0	60	20	9	2	0	0
1989–1993	63	24	12	4	0	0	64	17	14	3	2	0
1994–1998	68	31	16	1	0	0	70	33	13	1	2	0
1999–2003	72	43	19	4	0	0	77	43	16	3	1	0
Finland												
1964–1968	2	2	2	0	0	*	3	5	0	0	0	*
1969–1973	8	0	3	0	0	*	11	2	7	0	13	*
1974–1978	25	2	4	0	0	*	39	5	1	3	0	*
1979-1983	41	14	6	1	0	*	58	12	5	4	0	*
1984–1988	57	28	12	3	5	*	68	20	12	2	0	*
1989-1993	72	33	16	0	0	*	72	44	21	6	0	*
1994–1998	69	44	10	4	0	*	80	50	23	2	0 0	0
1999-2003	74	44	17	5	0	*	81	53	25	2 4	0	0
Iceland	11	11	17	5	0		01	55	21	1	0	0
1964-1968	13	*	12	*	*	*	8	*	*	*	*	*
1060_1073	13	*	12	*	*	*	8	*	*	*	*	*
1909-1975	25	*	10	*	*	*	31	0	*	*	*	*
1070_1083	35	*	10	*	*	*	31	0	*	*	*	*
1979-1985	56	12	10	*	*	*	02	67	11	*	0	*
1904-1900	50	13	9	*	*	*	00	0/ 67	11	*	0	*
1969-1995	20	15	17	*	*	*	03 72	0/ 51	11	*	*	*
1994-1998	89	*	17	*	*	*	/3	51	1	*	*	*
1999–2003	89		17				/3	51	1			
Norway	0	0	1	0	0	*	6	2	1	0	0	*
1964-1968	2	2	1	0	0	~	0	3	1	0	0	
1969–1973	15	6	I	0	0	0	22	4	3	0	0	~
1974-1978	33	13	8	1	0	~	38	4	1	1	0	0
1979–1983	48	14	4	0	0	0	58	6	4	4	3	
1984–1988	58	30	10	1	0		61	21	11	0	0	-
1989–1993	70	34	10	8	0	*	75	25	7	1	0	0
1994–1998	69	32	9	0	0	*	75	42	19	3	0	0
1999–2003	74	36	11	0	0	*	79	48	17	4	0	0
Sweden												
1964–1968	3	8	13	11	6	*	4	9	14	9	6	0
1969–1973	7	8	13	15	4	*	16	8	11	11	13	69
1974–1978	31	8	8	2	0	*	38	11	9	5	7	58
1979–1983	44	7	4	4	0	0	53	19	7	1	2	0
1984–1988	63	26	12	2	0	0	67	15	13	5	0	0
1989–1993	68	27	13	6	0	0	71	29	17	6	1	0
1994-1998	78	38	16	4	2	0	78	39	16	5	1	0
1999–2003	77	45	17	5	2	0	80	47	24	4	1	0

Table IX. Trends in 5-year age-specific relative survival in percent after acute leukaemia by sex and country. Nordic cancer survival study 1964–2003.

Numbers in *italics* indicate that two or more cells had to be combined to get sufficient number of patients to calculate survival. *Too few patients to calculate survival, see ref. [12].

pattern with respect to excess mortality for other cancer sites, reflecting that the time window shortly after diagnosis is very critical to prognosis. The increase in survival for all types of leukaemia can likely be ascribed to improved therapy, with chemotherapy the modality of choice. Evidently the crude division into acute and other leukaemia is insufficient for clinical purposes, and our results capture only the general observation of rapid and successful developments in treatment. The survival results we observe for acute leukaemia among younger patients predominantly reflect acute lymphocytic leukaemia (ALL) survival and among older patients those diagnosed with AML. For the other leukaemias, survival among the older age groups is dominated by CLL. It is well known that treatment regimes differ between the leukaemia subtypes, but for all, irrespective of the age of the patient, the focus is on the control of

710 H. H. Storm et al.

Table X. Trends in 5-year age-specific relative survival in percent after other leukaemia by sex and country. Nordic cancer survival study 1964-2003.

			Mei	1		Women						
Age	0–49	50–59	60–69	70–79	80-89	90+	0–49	50–59	60–69	70–79	80-89	90+
Denmark												
1964-1968	25	36	18	13	2	0	32	30	33	20	8	0
1969-1973	26	32	30	18	13	*	27	44	43	22	8	*
1974-1978	32	43	30	18	7	70	26	37	34	32	23	40
1979–1983	42	52	39	26	6	0	51	47	58	39	15	0
1984–1988	53	59	39	36	24	0	64	60	57	40	17	0
1989-1993	72	66	55	39	24	25	54	70	62	54	42	16
1994-1998	72	72	60	49	33	54	75	77	67	58	39	12
1999–2003	78	82	70	53	33	19	88	83	73	59	40	22
Finland												
1964-1968	19	36	30	23	11	*	29	28	35	20	10	*
1969-1973	21	43	32	22	0	*	21	47	43	30	36	*
1974-1978	40	51	46	33	11	0	49	50	52	38	19	*
1979–1983	37	52	48	48	17	0	43	55	59	47	35	0
1984–1988	51	56	57	40	17	96	52	68	65	47	28	30
1989-1993	65	71	63	42	17	0	62	66	55	55	24	0
1994-1998	69	71	60	48	22	0	71	72	59	46	26	18
1999-2003	80	74	65	40	22	0	81	74	72	51	22	6
Iceland												
1964-1968	13	13	13	23	0	*	21	21	21	22	*	*
1969–1973	13	13	13	23	0	*	21	21	21	22	*	*
1974-1978	35	35	35	26	32	*	52	52	52	20	47	*
1979–1983	35	35	35	26	32	*	52	52	52	20	47	*
1984–1988	51	51	51	45	90	*	60	60	60	64	0	*
1989-1993	82	82	82	34	51	*	60	60	60	64	0	*
1994-1998	74	74	74	65	40	*	74	74	74	38	46	*
1999-2003	<i>83</i>	83	83	69	33	*	73	73	73	62	60	*
Norway												
1964-1968	19	25	26	12	9	*	21	36	16	18	16	*
1969-1973	24	28	26	16	9	0	29	39	34	28	20	*
1974-1978	35	47	31	29	10	48	46	50	43	28	17	0
1979–1983	39	60	44	22	17	0	34	54	49	37	11	0
1984–1988	48	58	44	28	13	0	39	47	54	32	18	0
1989-1993	68	65	50	37	19	0	58	68	64	46	26	42
1994-1998	59	75	61	42	29	39	63	77	70	58	36	0
1999-2003	75	75	66	48	33	18	68	74	78	56	41	18
Sweden												
1964-1968	15	26	22	16	11	0	14	31	25	15	11	0
1969-1973	16	34	27	18	9	0	13	38	31	21	19	0
1974-1978	28	40	41	26	10	0	35	60	44	29	20	0
1979–1983	49	50	43	32	21	0	40	51	48	39	22	51
1984–1988	53	64	51	38	27	0	49	55	59	49	33	14
1989–1993	67	67	61	47	29	32	65	74	63	58	32	27
1994-1998	75	73	66	56	42	20	76	75	72	64	42	24
1999–2003	79	81	72	62	47	9	80	82	78	67	43	27

Numbers in *italics* indicate that two or more cells had to be combined to get sufficient number of patients to calculate survival. ^{*}Too few patients to calculate survival, see ref. [12].

the systemic disease. More recent successful treatment regimes e.g. for chronic myeloid leukaemia (CML), where imatinib (Gleevec) is the current treatment of choice [20], offer the promise of further improvement in leukaemia survival. The latter is believed to explain a marked increase in the median survival of CML, an observation that is unlikely to be picked up in a future study given that CLL dominates the other leukaemia group, but could be studied using the sub-typing of leukaemias usually available today in the cancer registries [20]. The classifications in the past of lymphomas and leukaemias alongside the changes in diagnostic precision will influence the survival trends, and a proper analysis on subtypes should be combined with quality control and a complete revision of data and the pathology for the entire time period under study.



Figure 9. Trends in age-standardised (ICSS) excess death rates per 100 person years for acute leukaemia by sex, country, and time since diagnosis in Nordic cancer survival study 1964–2003.

In conclusion, the lymphoid and haematopoietic cancer incidence, mortality and survival in the Nordic countries are much more similar than is seen for many other cancer forms. This may be expected given the nature of the diseases and that the first-line treatment is often systemic. We do however observe a general pattern that Danish patients with these diseases fare a little worse than their Nordic neighbours. The excess mortality rates for Danish patients one to three months after diagnosis rank highest, and role of co-morbidity related to lifestyle factors and its contribution to the success of chemotherapy and radiation should be considered in further studies.

Acknowledgements

The Nordic Cancer Union (NCU) has financially supported the development of the NORDCAN database and program, as well as the survival analyses in this project.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

References

- [1] Engholm G, Ferlay J, Christensen N, Bray F, Gjerstorff ML, Klint Å, et al. NORDCAN: Cancer incidence, mortality and prevalence in the Nordic countries, Version 3.4. Association of Nordic Cancer Registries. Danish Cancer Society. 2009 Available from http://www.ancr.nu.
- [2] Hartge P, Wang SS, Bracci PM, Devesa SS, Holly EA. Non-Hodgkin lymphoma. In: Schottenfeld D, Fraumeni JF Jr, editors. Cancer epidemiology and prevention. 3rd ed. New York: Oxford University Press; 2006. pp. 898–918.
- [3] Ekström-Smedby K. Epidemiology and etiology of non-Hodgkin lymphoma – a review. Acta Oncol 2006;45:258–71.
- [4] Mueller NE, Grufferman S. Hodgkin lymphoma. In: Schottenfeld D, Fraumeni JF Jr, editors. Cancer epidemiology and prevention. 3rd ed. New York: Oxford University Press; 2006. pp. 872–97.
- [5] Sant M, Allemani C, Santaquilani M, Knijn A, Marchesi F, Capocaccia R; the EUROCARE Working Group. EURO-CARE-4. Survival of cancer patients diagnosed in 1995-1999. Results and commentary. Eur J Cancer 2009;45: 931–91.
- [6] Engeland A, Haldorsen T, Tretli S, Hakulinen T, Hörte LG, Luostarinen T, et al. Prediction of cancer mortality in the Nordic countries up to the years 2000 and 2010, on the basis of relative survival analysis. A collaborative study of the five Nordic Cancer Registries. APMIS Suppl. 1995;49:1–161.
- [7] Møller B, Fekjaer H, Hakulinen T, Tryggvadóttir L, Storm HH, Talbäck M et al. Prediction of cancer incidence in the



Figure 10. Trends in age-standardised (ICSS) excess death rates per 100 person years for other leukaemia by sex, country, and time since diagnosis in Nordic cancer survival study 1964–2003.

Nordic countries up to the year 2020. Eur J Cancer Prev 2002;11(Suppl 1):S1–S96.

- [8] Roos AJ, Baris D, Weiss NS, Herrington L. Multiple myeloma. In: Schottenfeld D, Fraumeni JF Jr, editors. Cancer epidemiology and prevention. 3rd ed. New York: Oxford University Press; 2006. pp. 919–45.
- [9] Curado MP, Edwards B, Shin HR, Storm H, Ferlay J, Heanue M, et al., editors. Cancer incidence in five continents. Vol IX, Lyon, France: IARC Scientific Publications 160; 2007.
- [10] Linet M, Devesa SS, Morgan GJ. The leukemias. In: Schottenfeld D, Fraumeni JF Jr, editors. Cancer epidemiology and prevention 3rd ed. New York: Oxford University Press; 2006. pp. 841–71.
- [11] Engholm G, Storm HH, Ferlay J, Christensen N, Bray F, Ólafsdóttir E, et al. NORDCAN: Cancer incidence and mortality in the Nordic countries Acta Oncol 2010.
- [12] Engholm G, Gislum M, Bray F, Hakulinen T. Trends in the survival of patients diagnosed with cancer in the Nordic countries 1964–2003 followed up the end of 2006. Material and methods. Acta Oncol; 2010.
- [13] Brenner H, Rachet B. Hybrid analysis for up-to-date longterm survival rates in cancer registries with delayed recording of incident cases. Eur J Cancer 2004;40:2494–501.

- [14] Corazziari I, Quinn M, Capocaccia R. Standard cancer patient population for age standardising survival ratios. Eur J Cancer 2004;40:2307–16.
- [15] Talbäck M, Rosén M, Stenbeck M, Dickman PW. Cancer patient survival in Sweden at the beginning of the third millennium—predictions using period analysis. Cancer Causes Control 2004;15:967–76.
- [16] Nordic Myelomatosis Study Group. Nordic reference programme on Myelomaosis diagnosis and treatment 2001. Cited 30.11.2009. Available from http://www.nordic-myeloma.org/content/dk/pdf/ referenceprogrammer/referenceprogram_ 2001.pdf.
- [17] Smith A, Wisloff F, Samson D. Guide on the diagnostics and management of multiple myeloma 2005. Br J Haematol 2005;132:410–51.
- [18] Lund EM, Clemmensen IH, Storm HH, Engholm G. Survey of the Nordic Cancer Registries, Danish Cancer Society, Copenhagen 2000. Available from http://www.ncu.nu/ancr/ pdf/survey.pdf 29-08-2009.
- [19] Barlow L, Westergren K, Holmberg L, Talbäck M. The completeness of the Swedish Cancer Register: a sample survey for year 1998. Acta Oncol 2009;48:27–33.
- [20] Thygesen LC, Nielsen OJ, Johansen C. Trends in adult leukaemia incidence and survival in Denmark, 1943–2003. Cancer Causes Control 2009;20:1671–80.