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Trends in the overall survival of cancer patients diagnosed 1964–2003 in the Nordic countries followed up to the end of 2006: The importance of case-mix

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Abstract

Aim. Overall survival after cancer is frequently used when assessing the health care service performance as a whole. While used by the public, politicians, and the media, it is often discarded by clinicians and epidemiologists due to the heterogeneous mix of different cancers, risk factors and treatment modalities. We studied the trend in the Nordic 5-year relative survival and excess mortality for all cancers combined to see if the impact of case-mix and variations between countries in diagnostic methods such as breast screening and PSA testing could explain the lower survival in Denmark. *Material and methods*. From the NORDCAN database 1964–2003, we defined two cohorts of cancer patients, one excluding non-melanoma skin cancer and another also excluding breast and prostate cancer. 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*. Prostate cancer is the main driver of the incidence increase in men, as do breast cancer in women, whereas cancer mortality in all Nordic countries is declining. The 5-year relative survival ratios are increasing in each Nordic population, but less so in Denmark. Country differences in survival stem mainly from follow-up periods immediately after diagnosis. Adjusting for the case-mix of diagnoses diminished differences a little while exclusion of breast and prostate cancer reduced the gap between countries in survival and excess mortality more considerably, yet post-adjustment, Danish patients still fare worse during the first three months after diagnosis. *Conclusion*. Adjustment for case-mix and exclusion of sites where diagnostic procedures change the pattern of incidence is important when comparing overall cancer survival across countries, but the correction only explains part of the observed differences in survival. Other factors such as stage at presentation, co-morbidity, tobacco and alcohol consumption are likely contributors.

Cancer is a growing problem in the modern world, with increases both in incidence and mortality. Cancer control planning has long been established as a necessity in order to meet the demands of effective cancer control. Cancer control plans since the first WHO manual in 1992 have concerned the problems in both the developing [1,2] and in developed countries [3]. Well-established population-based monitoring systems of cancer incidence and mortality are essential in order to perform situation analysis on cancer and provide a tool for proper follow-up at the population level of actions taken following the establishment of cancer plans. Population-based estimates of incidence, mortality, survival, and to some extent prevalence, are necessary in this respect [4], and all of these measures in combination are needed to provide effective cancer control actions on the heterogeneous diseases combined into the single entity of cancer.

The Nordic countries, with their long tradition of high quality cancer registration based on effective and rather similar health care systems with equal and free access for their citizens, can provide the data needed to establish and monitor cancer control actions. They are also amongst the highest-resourced

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in the world, with a long tradition for high quality clinical and epidemiological research, as well as national centralised registration of all citizens based on unique ID numbers. It is possible to learn both from survival studies, from randomised clinical series assessing the effectiveness of treatment, and from population-based studies evaluating health care planning and resource allocation. It is thus possible to demonstrate what has been and what may be achieved at the population level when allocating best practice to the different types of cancer.

The EUROCARE studies [5,6] as well as earlier reports on cancer survival in the Nordic countries [7–12] demonstrated survival for specific cancer sites was below that observed in clinical randomised trials. Randomised clinical trials are conducted on carefully selected patients fulfilling preset criteria to minimise differences in the study arms other than the intervention under study, and such patients rarely reflect the general population composition with respect to age, co-morbidities, and other factors influencing survival. Clinicians unfortunately tend to discard the findings from the observational population-based series due to the obvious limitations with crude classifications, lack of detailed stage and treatment information, and suspected lack of comparability across health care systems and national borders. As Berrino et al. [4] state, clinicians often forget the relevance of the population-based survival as a way of benchmarking their own performance, while politicians and administrators under-appreciate the value of population-based estimates when setting provisions for cancer care and deciding resource allocation, given a growing and longer-living cancer patient population, coupled with the emerging need for targeted and expensive therapies.

Both the Nordic and the EUROCARE studies demonstrate variations in country-specific survival for many cancer sites and for all cancers combined. As a general feature, Denmark has a lower survival compared to the other Nordic countries, but at a level comparable to the survival in the UK [5]. This has led to a number of studies attempting to explain the reasons behind the differences. Dickman et al. [13] estimated the potential impact of reducing regional and social class variation; Robinson et al. [14] interpreted the effect of incomplete registration and the effect of cases based on death certificate only. However, neither regional differences nor technical aspects could explain the observed survival differences. Stage of cancer is established as an important predictor of survival, and even if stage is heterogeneously reported and missing for a high proportion of reported cases, adjustment for stage does not appear to fully account for the differences in survival [8]. Morphology, as reported to the cancer registries, has been studied for lung cancer but did not explain the survival discrepancies [10]. However in a breast cancer study, most of the observed survival variations between Denmark and Sweden were explained by adjusting for stage, diagnostic method, and patho-anatomical prognostic variables [11,12].

Epidemiologists and clinicians acknowledge that cancer as a single entity is problematic due to the complex mixture of different cancer types and subtypes with varying underlying risk factors, diagnostic methods and therapies. For these reasons the measures of overall incidence, mortality and survival attract limited professional interest. However, it must be realised that the public, journalists, politicians, and administrators often see this differently and take a general view of cancer when assessing the cancer burden and impact of cancer control plans, and use summary measures such as overall survival. Cancer plans are now developed or being developed in many countries – including the Nordic populations. When studying cancer within a country or administrative area via internal comparisons, many of the quality issues may be less important. However, when benchmarking is made across administrative borders – between countries, for example – it is very important that data are comparable. The purpose of the NORDCAN database and program is to provide as comparable data as possible from the Nordic countries and to make the results and underlying data available to all potential users [15]. Neither epidemiologists nor clinicians place a major emphasis on the group "all cancers" and hence only brief reports on this entity appear [5]; however, we analysed the overall cancer survival in the Nordic countries to evaluate the validity of this measure. An emphasis was placed on the case-mix of diagnoses (i.e. the variation between countries in the distribution of incidence of cancers that differ in terms of lethality) and the impact of screening for breast cancer and increased diagnostics resulting from use of the prostate specific antigen (PSA) test for prostate cancer, in order to visualise the collective impact on the interpretation of the trends in overall survival after a cancer diagnosis.

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. [15,16]. We included all cancers for patients diagnosed 1964–2003 with malignant neoplasms (ICD 10: C00-C95 + D09.0 + D41.4 + D32-33 + D42-43) excluding non-melanoma skin cancer (ICD10: C44 + C46.0) in Denmark, Finland, Iceland, Norway, and Sweden, and supplemented the cancer records

with individual records for death and emigration up to the end of 2006.

The data were analysed in two ways, first for all cancer sites excluding non-melanoma skin cancer and second for all cancer sites excluding non-melanoma skin cancer, prostate and breast cancer. The case-mix was considered since the frequency distribution of cancer sites deviate between countries; for instance, rectal cancer has been less frequent in Iceland and more frequent in Norway. Prostate cancer incidence has changed radically in some countries in the last two decades due to an increased use of PSA tests and subsequent biopsies, but less so in Denmark than in the other Nordic countries [17]. Breast cancer incidence is influenced by screening with a peak in incidence due to earlier diagnosis following the start of screening in the screened age groups. The start of breast cancer screening varied between countries, and by the end of the study period in 2003, it was still only offered in four of 16 counties in Denmark. With this in mind, a common weighting of cancer sites, a case-mix adjustment, should be used when comparing survival for summary groups between countries. We used as weights the Nordic distribution of the 15 most common cancer sites and the residual group of cancers in the last 5-year period 1999–2003 for each sex. Two sex-specific weight distributions for the two different summary groups *all cancer sites but non-melanoma skin* and *all cancer sites but non-melanoma skin, prostate, and breast cancer* as can be seen in Table I.

As described in detail elsewhere [18], 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 and cohort survival in the last period 1999–2003 [19]. Country-specific life tables were used to calculate the expected survival. Age standardisation was performed using the standard weight distribution for cancers more common among the elderly (ICSS standard number 3) as in the EUROCARE-4 analysis [20]. 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 diagnosis: the first month, 1–3 months, 4–12 months and yearly intervals thereafter. We present age-standardised (World) incidence and mortality rates, age-standardised (ICSS) 5-year relative survival ratios and excess mortality rates for the follow-up periods, the first month, 1–3 months, and 2–5 years following diagnosis, as well as age-specific 5-year relative survival ratios by country, sex, and age taking case-mix into account. The analysis of all sites combined without adjustment for case-mix is presented by Engholm et al. [18].

Table I. Weights (%) used in case-mix adjustment of cancer sites for 5-year relative survival for the summary groups *All cancer sites but non-melanoma skin* (W_1) and *All cancer sites but non-melanoma skin, prostate and breast cancer*(W_2) by sex. Nordic cancer survival study 1964–2003.

	Men		Women	
Cancer sites	W_1	W_2	W_1	W_2
Oesophagus	1.4	2.0	–	–
Stomach	3.0	4.3	2.0	2.9
Colon	7.3	10.6	8.3	11.9
Rectum	5.1	7.4	4.2	6.0
Liver	–	1.6	–	–
Pancreas	2.5	3.5	2.8	4.0
Lung	11.3	16.1	7.3	10.6
Breast			30.3	–
Cervix			2.5	3.5
Corpus			5.8	8.4
Ovary			4.3	6.2
Prostate	30.4	–		
Testis	1.7	2.3		
Kidney	2.5	3.6	1.8	2.6
Bladder	7.6	11.2	2.8	4.0
Melanoma	3.9	5.6	4.4	6.2
Brain	2.9	4.1	3.7	5.2
Thyroid	–	–	1.3	1.9
Non-Hodgkin lymphoma	3.5	5.0	3.2	4.5
Multiple myeloma	1.3	1.9	–	1.8
Other leukemia	1.7	2.5	–	–
Other cancer	14.0	18.4	15.5	20.4

Results

Excluding non-melanoma skin cancer, a total of 1 678 631 cancers among men and 1 681 766 among women were included in the study of all cancers. Excluding prostate and breast cancer, the total number of cases among men was reduced by 21.6% to 1 316 724 and among women by 25.9% to 1 246 873. Figure 1 presents the incidence, mortality and survival for *all cancer sites but non-melanoma skin* for men and women, and Figure 2 the equivalent but also excluding breast and prostate cancer. Over the entire study period, incidence was increasing, however for men it is evident on comparing Figures 1 and 2 that much of the increase since the mid-1980s was due to increasing incidence of prostate cancer. Denmark has the highest incidence in 1994–2003 when prostate cancer is excluded, whereas both Norway and Iceland have a higher total cancer incidence than Denmark when prostate cancer is included. It is noteworthy that the incidence of all cancer is declining from 1974 onwards in Finland when prostate cancer is excluded, as is the case for Sweden since the mid-1980s. The exclusion of the mortality of prostate cancer had no impact on the observed cancer mortality pattern between countries. Similarly it is clear that breast cancer was the driving force behind the increasing female incidence rates, however even on excluding breast cancer, incidence still rose, with the highest incidence in Denmark and

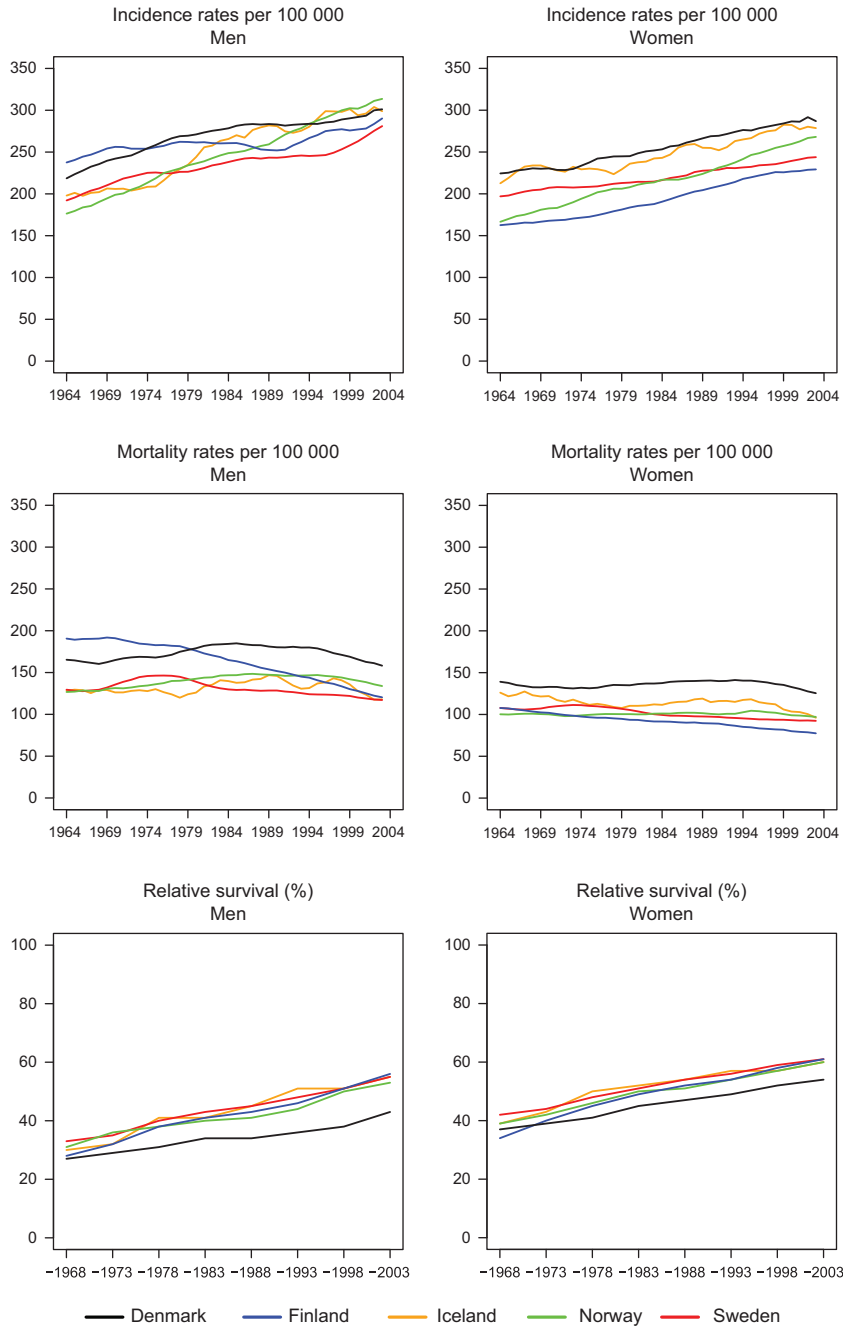

Figure 1. Trends in age-standardised (World) incidence and mortality rates per 100 000 and age-standardised (ICSS) 5-year relative survival for *all cancer sites but non-melanoma skin* (case-mix adjusted) by sex and country. Nordic cancer survival study 1964–2003.

Iceland, and the lowest rates in Finland. The cancer mortality among women is lower when breast cancer is excluded, with no change in the order of magnitude of the rates between countries.

The 5-year relative survival ratio is increasing during the observation period for all countries. Trends however, are quite different in men when prostate is excluded and in women when breast cancer is excluded, although to a lesser extent. The lower 5-year relative survival in Denmark among men is dramatic and difference increasing over time compared to the other Nordic countries. When prostate cancer is excluded the lower Danish survival is observed from the early-1980s, but the absolute differences in survival are not increasing markedly over time. For women the survival levels are lowered almost equally in all Nordic countries when breast cancer is excluded, however, the gap between Denmark and the other countries remains and appears to be increasing.

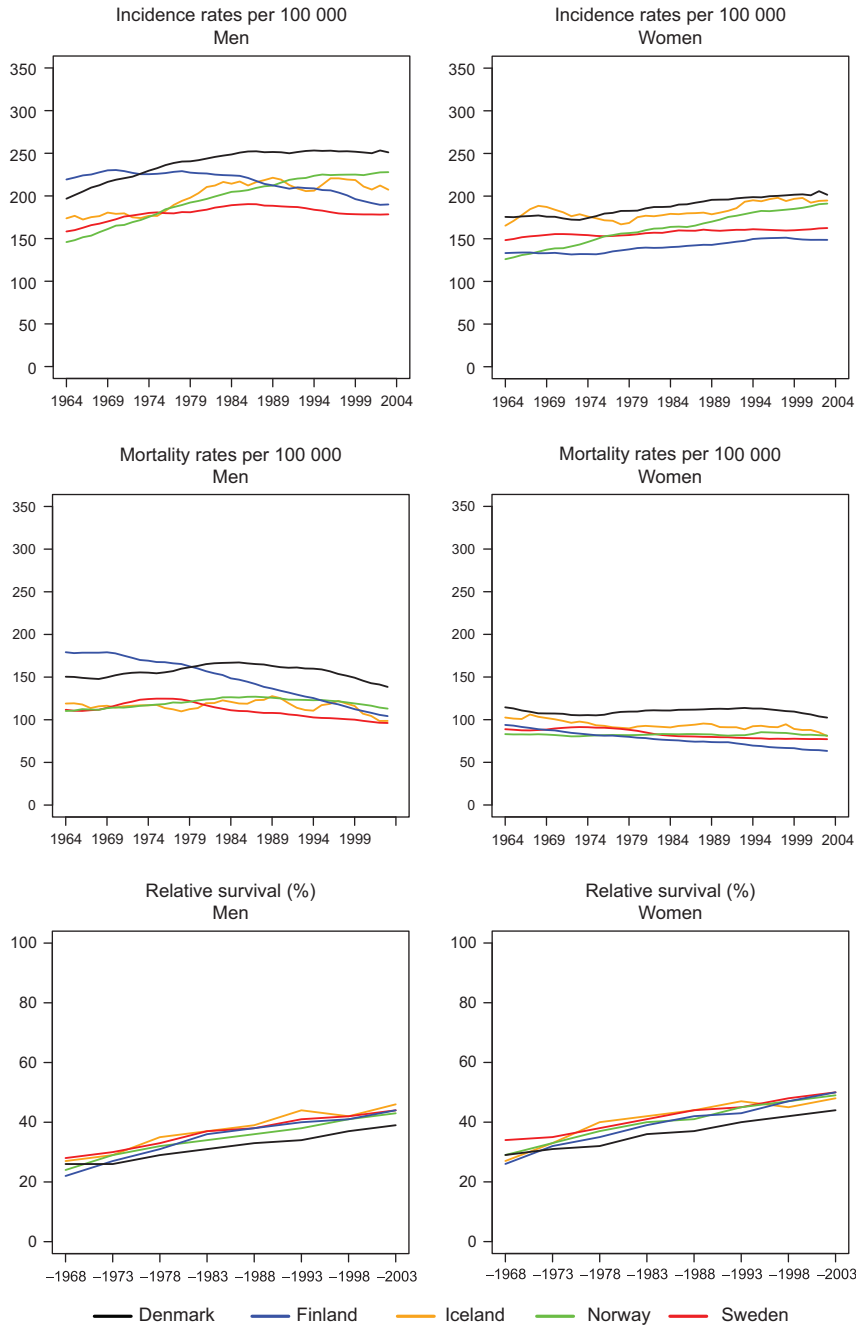

Figure 2. Trends in age-standardised (World) incidence and mortality rates per 100 000 and age-standardised (ICSS) 5-year relative survival for *all cancer sites but non-melanoma skin, prostate, and breast cancer* (case-mix adjusted) by sex and country. Nordic cancer survival study 1964–2003.

Tables II and III give the actual numbers, and show that the 8 to 15 percentage point difference between countries, with lower survival among men in Denmark compared to the other Nordic populations in 1989–1993 has become greater in 1999–2003 compared to Finland and Norway, at the same level compared with Sweden, and reduced slightly relative to Iceland. After excluding prostate cancer, the difference in relative survival was 4–10 percentage points in 1989–1993, and 4–7 percentage for the most recent period 1999–2003. For women, the 3–8 percentage point difference is relatively stable over time, irrespective of whether breast cancer is included or not.

Tables IV and V present the 5-year relative survival ratios by age groups. The 5-year relative survival is highest among the younger male patients (<60 years) and ranges from 61–65% during 1999–2003

Table II. Trends in survival *for all cancer sites but non-melanoma skin* (case-mix adjusted) 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)	N	RS (CI)	N	RS (CI)	N	RS (CI)
Men										
1964–1968	33 821	27 (26–28)	25 941	28 (27–30)	885	30 (25–36)	23 636	31 (29–32)	59 561	33 (32–34)
1969–1973	40 489	29 (28–30)	28 844	32 (31–33)	1 050	32 (28–36)	27 360	36 (34–37)	69 089	35 (34–36)
1974–1978	46 267	31 (30–32)	31 449	38 (37–39)	1 262	41 (37–44)	33 004	38 (37–39)	70 536	40 (39–40)
1979–1983	50 317	34 (33–36)	34 962	41 (40–43)	1 636	41 (38–44)	37 081	40 (39–41)	75 593	43 (42–43)
1984–1988	52 765	34 (34–35)	38 072	43 (42–44)	1 888	45 (42–48)	40 822	41 (40–42)	84 377	45 (44–45)
1989–1993	54 531	36 (35–37)	40 609	46 (45–47)	2 123	51 (47–55)	44 998	44 (44–45)	90 094	48 (47–48)
1994–1998	57 239	38 (38–39)	48 966	51 (50–52)	2 557	51 (48–54)	49 899	50 (49–51)	94 799	51 (51–52)
1999–2003	62 985	43 (42–44)	55 042	56 (56–57)	2 796	55 (53–58)	54 144	53 (53–54)	107 142	55 (55–55)
Women										
1964–1968	36 988	37 (36–37)	24 331	34 (33–35)	1 098	39 (35–43)	24 078	39 (38–40)	61 974	42 (42–43)
1969–1973	41 367	39 (38–39)	26 567	40 (39–41)	1 205	43 (39–47)	26 916	42 (41–43)	69 179	44 (44–45)
1974–1978	47 170	41 (41–42)	30 370	45 (44–46)	1 379	50 (47–53)	31 537	46 (45–47)	70 544	48 (48–49)
1979–1983	51 433	45 (44–45)	35 424	49 (48–50)	1 610	52 (49–55)	35 289	50 (49–50)	75 929	51 (51–52)
1984–1988	54 691	47 (46–47)	40 787	52 (51–53)	1 886	54 (51–57)	38 431	51 (50–52)	82 242	54 (53–54)
1989–1993	59 097	49 (49–50)	45 485	54 (53–54)	2 015	57 (54–59)	41 714	54 (54–55)	88 895	56 (56–56)
1994–1998	63 087	52 (52–53)	50 869	58 (57–58)	2 407	57 (54–59)	46 315	57 (57–58)	93 489	59 (59–59)
1999–2003	68 048	54 (54–55)	54 986	61 (61–62)	2 690	60 (58–62)	51 162	60 (59–60)	99 082	61 (60–61)

in all countries but Denmark, where it reaches 49%. The differences in survival are only marginally lower among the older patients, with a survival of 32% among 80–89 year old male patients in Denmark compared to between 39% and 46% in the other countries, also in the last period. Excluding prostate cancer, the levels of 5-year survival for male patients diagnosed at ages under 50 1999–2003 range from 58 to 65%, with Denmark at 54%, and for ages 80–89, between 30% and 35%, with Denmark at 26%. Comparing the two tables, it is evident that the exclusion of prostate cancer reduces the survival in all countries but less so in Denmark, with the exception of Danish and Icelandic men diagnosed at ages 0–49. For women, the survival pattern is similar to that among men, with the highest survival observed among the younger patients; with the exclusion of breast cancer, survival reduced 6–13 percentage points among women diagnosed below the age of 80 in all countries.

Table III. Trends in survival for *all cancer sites but non-melanoma skin, prostate, and breast cancer* (case-mix adjusted) 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)	N	RS (CI)	N	RS (CI)	N	RS (CI)
Men										
1964–1968	30 190	26 (25–26)	23 928	22 (21–23)	780	27 (23–32)	19 089	24 (23–25)	47 260	28 (27–29)
1969–1973	36 235	26 (26–27)	25 863	27 (26–28)	906	29 (26–33)	22 149	29 (28–30)	54 123	30 (29–30)
1974–1978	40 955	29 (29–30)	27 608	31 (30–32)	1 046	35 (32–39)	26 295	32 (31–33)	54 467	33 (32–33)
1979–1983	43 938	31 (31–32)	29 934	36 (35–37)	1 309	37 (34–40)	29 412	34 (34–35)	57 385	37 (36–38)
1984–1988	45 941	33 (32–33)	32 089	38 (37–39)	1 468	39 (36–42)	32 196	36 (35–37)	62 611	38 (38–39)
1989–1993	47 213	34 (34–35)	32 805	40 (39–40)	1 599	44 (41–47)	34 627	38 (38–39)	64 981	41 (40–41)
1994–1998	49 623	37 (36–37)	35 802	41 (41–42)	1 848	42 (39–45)	37 082	41 (40–41)	65 683	42 (42–43)
1999–2003	52 514	39 (38–39)	36 751	44 (43–45)	1 928	46 (44–48)	39 241	43 (42–43)	67 850	44 (43–44)
Women										
1964–1968	28 478	29 (29–30)	19 860	26 (26–27)	855	27 (24–31)	18 357	29 (28–30)	47 203	34 (33–34)
1969–1973	31 779	31 (30–31)	20 936	32 (31–33)	958	33 (30–36)	20 631	33 (32–34)	52 406	35 (35–36)
1974–1978	35 619	32 (32–33)	23 432	35 (34–36)	1 041	40 (36–44)	24 181	37 (36–38)	51 841	38 (38–39)
1979–1983	39 347	36 (35–36)	27 216	39 (39–40)	1 219	42 (39–46)	27 264	40 (39–40)	55 619	41 (41–42)
1984–1988	41 214	37 (37–38)	30 277	42 (41–43)	1 376	44 (41–47)	29 542	41 (41–42)	60 406	44 (43–44)
1989–1993	44 021	40 (39–40)	32 851	43 (43–44)	1 498	47 (44–50)	32 168	45 (44–46)	63 890	45 (45–46)
1994–1998	46 400	42 (42–43)	36 006	47 (46–48)	1 782	45 (43–48)	35 060	47 (46–48)	66 379	48 (48–49)
1999–2003	49 039	44 (43–44)	37 698	50 (50–51)	1 924	48 (46–50)	38 224	49 (49–50)	68 876	50 (49–50)

Table IV. Trends in 5-year age-specific relative survival in percent after *cancer of all sites but non-melanoma skin* (case-mix adjusted) by sex and country. Nordic cancer survival study 1964–2003.

	Men						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	31	32	31	25	16	13	49	42	38	34	24	17
1969–1973	41	35	31	26	17	14	52	45	41	33	27	14
1974–1978	35	37	34	29	22	9	55	48	44	36	29	15
1979–1983	48	40	36	31	21	11	58	51	47	40	31	18
1984–1988	39	39	36	32	26	21	61	53	49	43	32	28
1989–1993	42	37	38	34	27	25	63	55	51	45	35	19
1994–1998	47	41	41	35	29	15	65	59	54	48	38	28
1999–2003	49	49	47	40	32	20	69	62	56	49	41	29
Finland												
1964–1968	41	35	31	24	12	0	51	43	36	29	16	40
1969–1973	36	37	35	30	21	16	56	47	42	34	26	67
1974–1978	46	44	40	35	27	30	61	51	47	40	32	25
1979–1983	47	46	45	40	28	18	65	55	50	45	34	36
1984–1988	45	47	46	42	34	25	69	59	54	46	37	28
1989–1993	49	48	48	43	39	25	70	63	56	48	38	32
1994–1998	55	58	54	48	40	35	73	68	60	51	41	27
1999–2003	64	62	59	53	46	38	76	70	64	55	46	38
Iceland												
1964–1968	17	38	36	21	38	37	50	47	40	35	24	0
1969–1973	25	30	38	34	23	0	60	52	41	34	39	0
1974–1978	30	50	51	37	28	40	61	59	49	45	43	13
1979–1983	39	42	49	39	31	4	67	60	53	45	41	13
1984–1988	35	54	54	36	43	12	67	62	55	46	47	44
1989–1993	59	55	48	51	45	45	72	59	60	56	38	43
1994–1998	48	63	52	50	40	33	72	65	57	52	43	20
1999–2003	61	65	58	50	46	31	76	67	62	54	45	38
Norway												
1964–1968	39	37	33	27	21	6	53	45	41	34	25	22
1969–1973	43	41	38	31	27	9	56	48	45	37	29	22
1974–1978	47	44	41	34	27	27	61	51	48	41	34	20
1979–1983	44	46	42	37	32	25	64	56	50	46	37	37
1984–1988	46	46	45	39	31	28	64	56	54	47	38	30
1989–1993	49	50	48	42	33	23	68	60	55	51	41	31
1994–1998	61	57	53	46	37	24	70	64	60	53	43	36
1999–2003	64	62	57	49	39	24	73	67	63	54	46	40
Sweden												
1964–1968	42	39	36	29	21	10	58	49	44	37	29	21
1969–1973	48	43	38	31	21	9	60	52	46	38	29	14
1974–1978	48	46	42	36	27	26	62	54	50	44	36	31
1979–1983	45	47	45	40	35	24	65	57	53	47	39	26
1984–1988	49	49	47	43	36	30	67	59	56	50	41	36
1989–1993	53	51	49	46	41	29	68	62	58	52	43	34
1994–1998	59	57	54	49	40	39	71	65	61	55	45	41
1999–2003	65	61	57	51	44	42	73	67	63	56	48	39

The excess mortality rates in the first month following diagnosis in Figures 3 and 4 show that the levels are high in the early years around 1970 for the summary group *all cancer sites but non-melanoma skin* and the levels decrease to about the half in the last period 1999–2003. The differences between countries peak in the 1970s, with Denmark and Sweden having the highest rates. Excess rates then decrease to about the same level in the last period, but with rates in Iceland and Sweden somewhat lower. The pattern is very similar for male and female patients, irrespective of whether prostate and breast cancers are excluded, – although the level for men change. In the second follow-up interval, the second and third month following diagnosis, a decrease in the excess rates is seen over time, but with a considerably lower level and trend than in the first interval. When studying all calendar years, the excess mortality is higher in Denmark than in the other countries. In the last interval shown in Figure 3, the interval 2–5

Table V. Trends in 5-year age-specific relative survival in percent after *cancer of all sites but non-melanoma skin, prostate, and breast cancer* (case-mix adjusted) by sex and country. Nordic cancer survival study 1964–2003.

	Men						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	36	33	27	22	15	18	42	37	31	25	16	15
1969–1973	38	33	27	22	15	7	45	39	32	25	18	10
1974–1978	41	34	31	25	20	9	48	40	34	26	19	5
1979–1983	44	38	33	27	20	10	51	43	38	30	22	12
1984–1988	46	39	33	28	23	17	54	44	40	32	23	17
1989–1993	48	39	36	31	23	22	56	47	41	34	26	19
1994–1998	51	43	37	32	25	13	59	50	43	37	28	23
1999–2003	54	44	40	34	26	16	62	52	45	37	29	20
Finland												
1964–1968	34	29	25	18	9	0	45	38	28	20	8	5
1969–1973	39	36	28	21	15	10	50	40	33	25	17	27
1974–1978	44	39	32	27	18	34	55	44	37	28	19	7
1979–1983	49	44	38	33	21	8	59	47	41	34	23	17
1984–1988	53	45	39	33	27	29	64	50	44	35	25	20
1989–1993	54	46	41	34	30	20	65	52	45	37	25	16
1994–1998	57	48	43	36	30	25	67	58	49	40	29	19
1999–2003	59	50	46	38	33	25	70	60	53	43	33	24
Iceland												
1964–1968	25	38	33	20	19	49	40	36	29	22	14	0
1969–1973	36	37	33	25	18	0	56	46	34	22	21	0
1974–1978	42	43	40	29	21	0	54	50	39	33	33	17
1979–1983	55	40	40	32	24	6	60	52	46	33	29	0
1984–1988	50	52	43	25	36	26	62	52	45	36	31	37
1989–1993	62	48	42	40	32	41	69	47	51	45	26	22
1994–1998	57	55	41	37	27	16	64	55	45	39	31	19
1999–2003	65	56	47	37	35	21	69	56	51	41	29	27
Norway												
1964–1968	33	30	24	20	18	5	45	38	31	24	15	7
1969–1973	39	34	30	23	23	9	49	41	36	26	19	12
1974–1978	48	40	34	26	21	16	54	43	39	31	23	21
1979–1983	50	42	35	28	24	18	57	48	41	34	26	20
1984–1988	50	43	38	31	23	24	58	50	44	35	26	24
1989–1993	52	45	41	33	25	18	63	53	46	40	29	20
1994–1998	55	48	42	35	28	21	64	55	49	42	31	26
1999–2003	58	51	44	37	30	20	67	57	52	43	34	30
Sweden												
1964–1968	40	36	30	23	16	12	51	43	35	26	20	11
1969–1973	44	38	31	25	17	6	53	45	37	28	20	11
1974–1978	45	40	35	27	21	26	55	47	40	32	24	19
1979–1983	50	41	38	33	28	15	59	48	43	36	26	18
1984–1988	52	44	39	34	27	21	62	51	45	38	29	21
1989–1993	54	46	41	37	32	22	62	53	46	41	31	24
1994–1998	57	48	43	38	31	28	65	55	49	43	34	30
1999–2003	59	50	44	39	34	28	67	57	51	44	37	28

years after diagnosis, the levels of excess mortality conditional on the cancer patients surviving the first two years after diagnosis, are much lower, about 6–12 per 100 person-years, with little difference between the countries and a minor decreasing trend over time.

Adjusting for case-mix in the last period 1999–2003, the relative 5-year survival increase for all sites for Danish men (1 percentage points), had no impact on Finnish men, and decreased for Icelandic (2 percentage point), Norwegian (1 percentage point), and Swedish men (4 percent points) (Table VI). In women, the adjustment increased the survival in Denmark (2 percentage points), Iceland (3 percentage points), Norway (2 percentage points), and had no impact on the survival in Finland and Sweden. After removing prostate cancer from the all cancer group, adjustment for case-mix had no impact on the

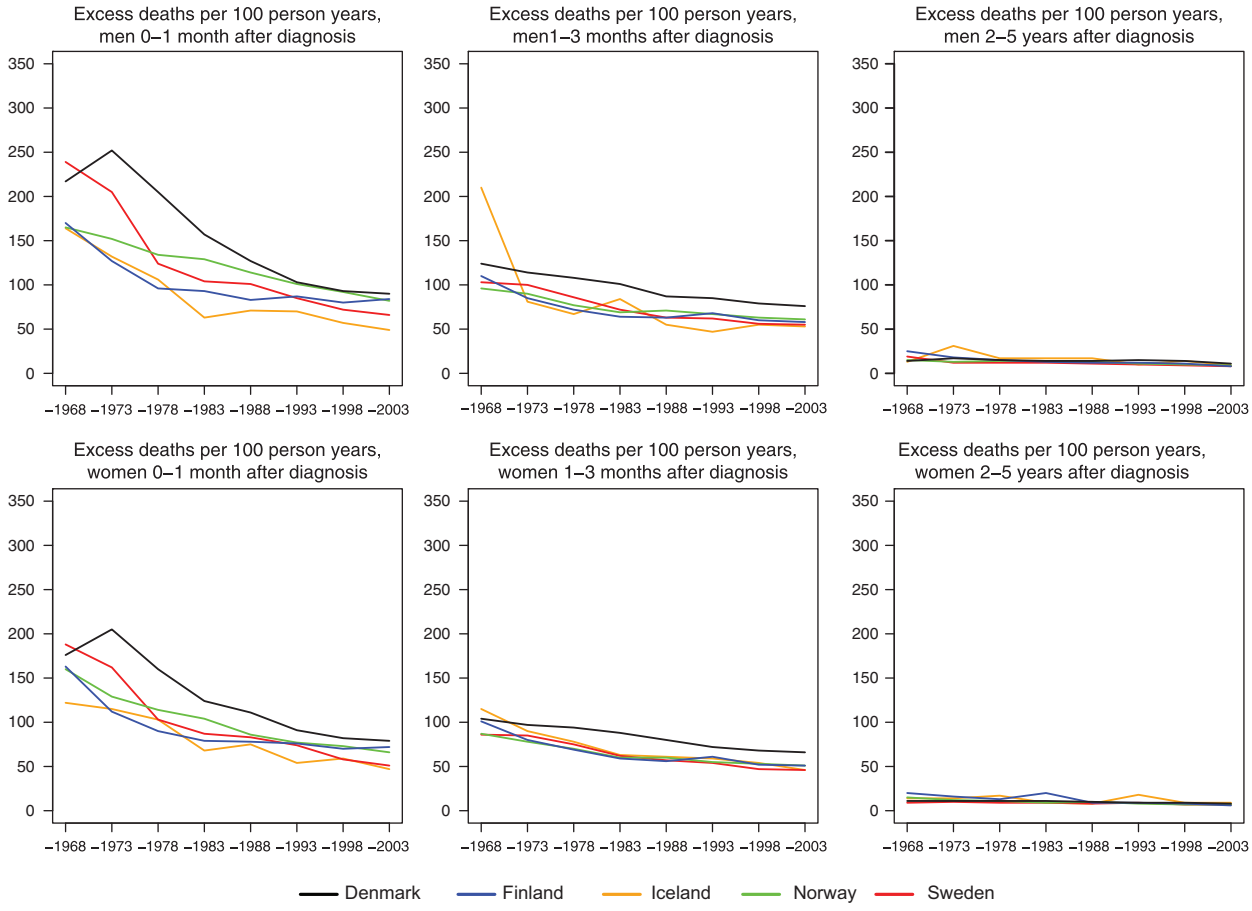

Figure 3. Trends in age-standardised (ICSS) excess death rates per 100 person years for *all cancer sites but non-melanoma skin* (case-mix adjusted) by sex, country, and time since diagnosis in Nordic cancer survival study 1964–2003.

Danish survival but increased survival by 4 percent points in Finland and 1 percent point in Iceland, and lowered survival in both Norway and Sweden. In women, the survival increased with case-mix in Denmark and Iceland when breast cancer was removed from the all-cancers figure, and decreased in Finland, Sweden, and Norway.

Discussion

We have used the routinely-collected incidence and mortality data delivered by the Nordic cancer registries to the NORDCAN database [16] to conduct a comprehensive situation analysis on cancer in the Nordic countries, an action recommended by the WHO for cancer control monitoring [3]. Although such summarised data may be of lesser relevance to clinicians from a public health perspective, it is considered of value as a benchmarking exercise examining the performance of the health care system as a whole [4]. However, as quality and comparability of data are of concern, our results should interest all stakeholders in cancer control, both in the Nordic countries and elsewhere, inasmuch that the Nordic cancer registries are recognised for their high quality data, with national central population registries and a unique ID given to every citizen, and where reliable follow-up for vital status can be made using register linkages, thus avoiding biases seen elsewhere from a failure to adequate follow-up or link the relevant data.

In general, we found similar increases in the 5-year relative survival ratios in the Nordic countries from 1964–2003. The gap in survival between Denmark and the other Nordic countries demonstrated from the late 1970s may be considered to result from the growth of financial resources to health care slowing down in Denmark and a new agreement between the Medical Association and the hospital owners that introduced significant changes in working hours for doctors. This gap is still seen in patients diagnosed in 1999–2003, and to some extent the survival disparities have widened over the years, despite the changes introduced in health care in Denmark in relation to the development of the national cancer control plan (launched in 2000). One may argue that trends in and comparison of overall survival have little relevance since it is for an aggregated group of very different diseases, but the measure is of political

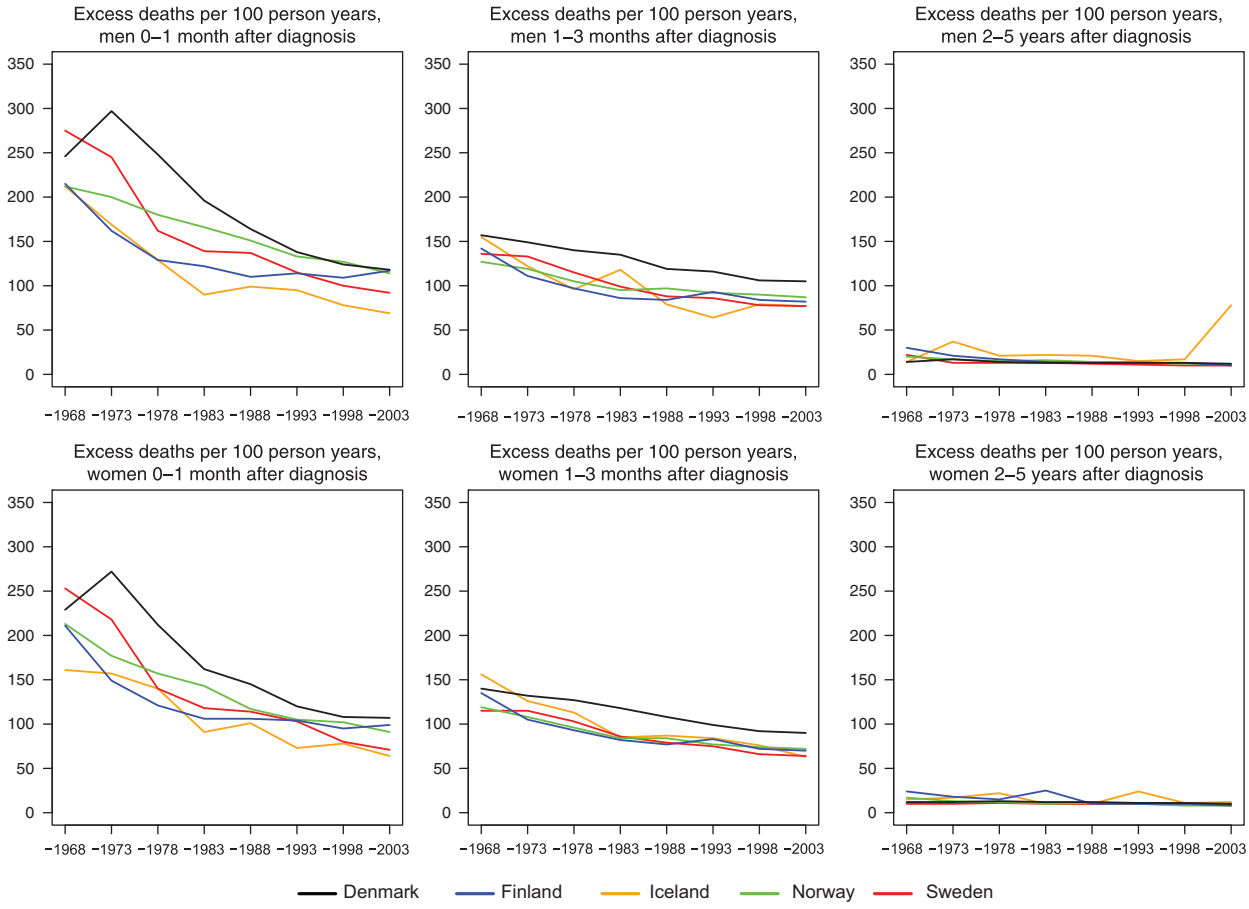

Figure 4. Trends in age-standardised (ICSS) excess death rates per 100 person years for *all cancer sites but non-melanoma skin, prostate, and breast cancer* (case-mix adjusted) by sex, country, and time since diagnosis in Nordic cancer survival study 1964–2003.

interest and has been accepted as an indicator for the overall performance of health care systems [4,6]. It is worthy of note, that the survival differences diminish when case-mix is taken into account, particularly for men when prostate cancer is excluded. This is not unexpected and has been discussed by Berrino et al. in a commentary on earlier EUROCARE results [4]. On the other hand, these findings raise a general warning as to the relevance of presenting and comparing overall survival ratios including all cancers, inasmuch that the results are heavily dependent on an in-depth knowledge of diagnostic methods, criteria and medical examination practices, as well as the potential for effective treatment regimens. For prostate cancer, the impact on variation in the use of PSA testing on incidence and survival are well-established [17], but differences in diagnostic intensity are likely for other primary sites as well – e.g. for colorectal cancers and the use of haemocult or endoscopic examinations as screening methods for early cancers [21,22]. For other sites such as cancers of the brain, it has been previously demonstrated [23] that the use of modern imaging techniques including CT and MR scans were introduced first for younger age groups and only after a period of time routinely offered to patients diagnosed at older ages.

It was expected, perhaps naively, that the Danish survival would have improved and converged towards the survival of the other Nordic countries following the initiation of the first Danish cancer plan in 2000 [24]. It could be argued that it is too early to pick up more recent changes, since only the latest three years of incidence data could have been influenced by improvements in treatment, with follow-up time equally short. However, it was clear already in 1998 [8] that a significant part of the survival deficit relates to the first year after diagnosis, and later publications [24–26] showed that this deficit primarily relates to the time window between diagnosis and six months follow-up. Differences in survival tend to diminish where patients have survived the first year [27]. It is thus possible to pick up improvements in diagnostics and treatment early by comparing survival and excess mortality within the first year after diagnosis, whilst waiting for the long-term results of prevention.

Even if survival levels differ between countries, the increase in survival after colorectal cancer in all the Nordic countries, a cancer site where the front-line therapy is surgery, is indicative of modern surgical techniques being implemented at the same pace in all countries. Likewise the similar survival in the Nordic countries observed for lymphomas, sites

Table VI. Number of tumours (N) and 5-year age-standardised (ICSS) relative survival in percent with 95% confidence intervals (RS (CI)) with and without case-mix for the summary group *all cancer sites but non-melanoma skin* and for the summary group when also excluding prostate cancer among men and breast cancer among women. Patients diagnosed 1999–2003 in the Nordic countries by sex.

All cancer sites but non-melanoma skin		Denmark		Finland		Iceland		Norway		Sweden	
		N	RS (CI)	N	RS (CI)	N	RS (CI)	N	RS (CI)	N	RS (CI)
Men											
Prostate included	Case-mix adjusted										
Yes	Yes	62 985	43 (42–44)	55 042	56 (56–57)	2 796	55 (53–58)	54 144	53 (53–54)	107 142	55 (55–55)
	No		42 (42–42)		56 (55–56)		57 (55–59)		54 (53–54)		59 (58–59)
No	Yes	52 514	39 (38–39)	36 751	44 (43–45)	1 928	46 (44–48)	39 241	43 (42–43)	67 850	44 (43–44)
	No		39 (38–39)		40 (40–41)		45 (43–47)		44 (43–44)		46 (46–46)
Women											
Breast included	Case-mix adjusted										
Yes	Yes	68 048	54 (54–55)	54 986	61 (61–62)	2 690	60 (58–62)	51 162	60 (59–60)	99 082	61 (60–61)
	No		52 (51–52)		61 (61–61)		57 (55–59)		58 (58–59)		61 (61–61)
No	Yes	49 039	44 (43–44)	37 698	50 (50–51)	1 924	48 (46–50)	38 224	49 (49–50)	68 876	50 (49–50)
	No		42 (42–43)		51 (51–52)		46 (44–48)		51 (50–51)		51 (51–52)

where chemotherapy remain the first choice, supports the view that chemotherapeutic drugs are provided and administered with rather similar levels of efficiency in all the countries.

In earlier publications, technical reasons for differences in survival have been studied that potentially explained the deficit in Denmark (e.g. regional variations, varying DCO proportions), although such contributions have been considered rather minor [13,14]. The only important factor may have been the lack of linkage in Sweden with the mortality register to follow-back on cases initially only reported on a death certificate [28]. Such a trace-back would likely lower the Swedish survival estimates, but only by a few percent points; even if this were to narrow the gap between Sweden and Denmark, it will not have had any impact on the other countries, where survival remains superior to that of Denmark. Differences in follow-up and missed linkages to mortality data are important issues to consider outside the Nordic area, leading to artificially-inflated survival – but with the use of the unique personal ID in all the Nordic countries, such artefacts are not likely to operate in this study.

The Danish deficit in survival may be considered a true observation, as is supported by the fact that Danish life expectancy has not improved at the same pace observed in the other Nordic countries [18], and is substantially lower at present. The population of Denmark, for example, has a life expectancy more than three years lower than that of Sweden – an observation almost exclusively explained by a higher tobacco and alcohol consumption in Denmark [29]. Since the excess mortality is about the same for the countries after approximately one year, the survival deficit must relate to patient or treatment characteristics close to the time of diagnosis. The survival in Denmark increases almost in parallel with that of the other Nordic countries, the same success – in relative terms – on introducing new therapies and other improvements in management is seen in Denmark as elsewhere. Comparing Denmark, Finland, and Norway – where stage information is included in the cancer registers – the Danes presented with more advanced disease, but had poorer absolute survival levels across stages, and hence adjustment for stage could not explain the overall survival differences [8]. Nevertheless, as stage is one of the most important predictors of survival [8,12,25] the unfavourable Danish stage distribution will be part of the explanation. In order to reduce late stage at presentation, it will be necessary to improve diagnostics considerably, establish organised screening programmes where these are proven cost-effective from a public health perspective, and increase awareness about signs and symptoms, both in the general population and among the medical profession.

A recent analysis of the incidence and survival patterns by socioeconomic position in Denmark showed that tobacco- and alcohol-related cancers were more prominent among the less advantaged socioeconomic groups [30]. Alcohol consumption is lower in Iceland, Norway and Sweden, and with respect to tobacco use, both Sweden and Iceland have low consumption, while smoking trends in Finland have declined rapidly since the 1970s to a level considerably lower than that of Denmark [27]. This may be one explanation for the inferior survival in Denmark, as co-morbidity, related to tobacco and alcohol and a generally poorer state of health will have an impact on the effectiveness of almost all therapeutic modalities. In addition, such risk factors provide the

patient with a poorer constitution whereby the tolerance of various therapies is reduced relative to more healthy individuals [31]. Given the obvious societal benefits of reducing tobacco and alcohol consumption in the population, it remains important to aggressively pursue primary prevention policies in each of the Nordic countries, particularly in Denmark.

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