

ORIGINAL ARTICLE

Trends in the survival of patients diagnosed with cancers of the lip, oral cavity, and pharynx in the Nordic countries 1964–2003 followed up to the end of 2006

TIMO HAKULINEN¹, LAUFHEY TRYGGVADÓTTIR^{2,3}, METTE GISLUM⁴,
HANS H. STORM⁴, FREDDIE BRAY^{5,6}, ÅSA KLINT⁷ & GERDA ENGHOLM⁴

¹Finnish Cancer Registry, Pieni Roobertinkatu 9, FI-00130 Helsinki, Finland, ²Icelandic Cancer Registry, Reykjavik, Iceland, ³Department of Medicine, University of Iceland, Reykjavik, Iceland, ⁴Department of Cancer Prevention and Documentation, Danish Cancer Society, Copenhagen, Denmark, 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 ⁷Swedish Cancer Registry, National Board of Health and Welfare, Stockholm, Sweden

Abstract

Background. This is the first comprehensive population-based study on relative survival of lip, oral cavity and pharyngeal cancer in the Nordic countries. **Material and methods.** Relative survival of patients with cancers of the lip, oral cavity, and pharynx diagnosed in the Nordic countries in 1964–2003 and followed up to the end of 2006 was studied and contrasted with trends in incidence and mortality. **Results.** There are marked differences in incidence between countries and over time. The stability of the relative survival ratios gives support to the hypothesis that the incidence differences are more likely to be real and not materially affected by differences in definitions and coding. Of particular note are the steep rises in pharyngeal cancer incidence in Denmark in both sexes. Survival has only moderately improved over time and has tended to be slightly higher in females than males. **Conclusions.** Co-morbidity caused by smoking and high alcohol consumption are likely to be partially responsible for differences between countries. Advances in therapy and standards of care are also likely to have played a role in the increasing survival trends.

Key Words: *Relative survival, excess mortality, cancer registry, population-based, pharyngeal cancer*

In the Nordic countries, cancers of the lip, oral cavity, and pharynx are relatively rare, accounting for about 2% of all new cancer cases observed in the Nordic countries in 2002–2006 [1]. The main known risk factors are smoking, oral tobacco consumption and alcohol, but the role of these factors varies greatly between the anatomic locations and sexes [2]. These risk factors, particularly smoking, result in patient co-morbidity which may impact on the relative survival differences between population groups. The role of HPV infection has been established as a risk factor, particularly for oropharyngeal cancer [3].

Rather little has been published thus far on the population-based survival experience of head and

neck cancer patients in the Nordic countries. The EURO CARE studies [4,5] have shown that the Nordic relative survival figures (with the occasional exception of Denmark) are among the highest observed in Europe.

The aim of the present study is to describe and compare Nordic trends in relative survival and excess mortality of the patients from 1964–2003 to those of incidence and mortality, providing some basic interpretation of the findings.

Material and methods

The materials and methods are described in detail in an earlier article in this issue [6]. In brief, the

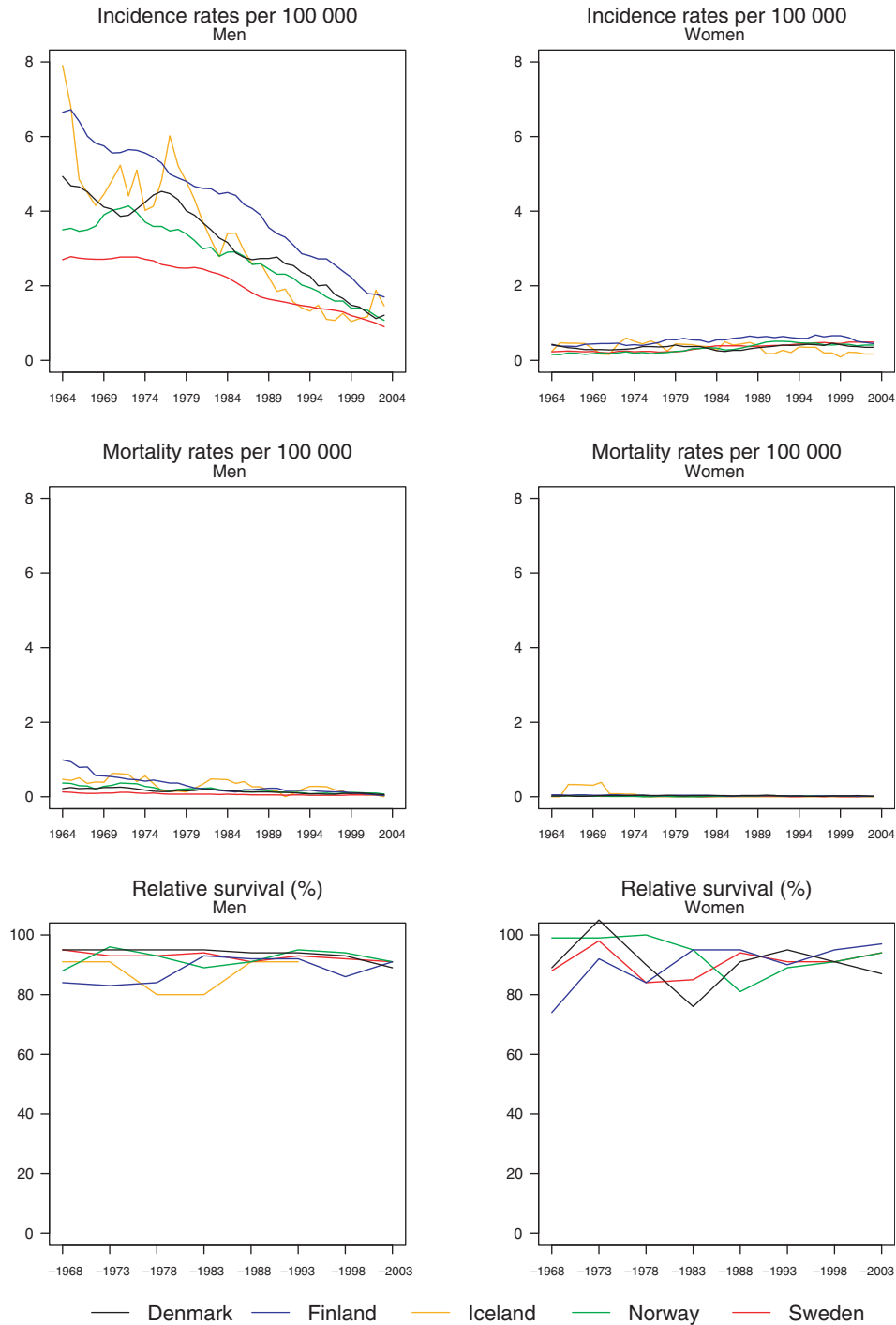


Figure 1. Trends in age-standardised (World) incidence and mortality rates per 100 000 and age-standardised (ICSS) 5-year relative survival for lip cancer by sex and country. Nordic cancer survival study 1964–2003.

NORDCAN database contains comparable data on cancer incidence and mortality in the Nordic countries, as delivered by the national cancer registries, with follow-up information on death or emigration for each cancer patient available up to and including 2006. Oral cavity and pharyngeal tumours were extracted according to ICD-10 for cancers of the lip (ICD-10 C00), tongue (ICD-10 C01-02), salivary

glands (ICD-10 C07-08), mouth (ICD-10 C03-06), and pharynx (ICD-10 C09-14).

Sex-specific 5-year relative survival was calculated for each of the diagnostic groups in each country for eight 5-year periods from 1964–1968 to 1999–2003. For the last 5-year period, so-called hybrid methods were used. Country-specific population mortality rates were used for calculating the

Table I. Trends in survival for lip cancer 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	735	95 (89–101)	716	84 (76–92)	24	<i>91 (76–109)</i>	460	88 (82–94)	808	95 (90–101)
1969–1973	642	95 (89–101)	659	83 (77–89)	29	<i>91 (76–109)</i>	576	96 (91–102)	868	93 (89–98)
1974–1978	792	95 (90–100)	675	84 (79–90)	31	<i>80 (65–97)</i>	535	93 (87–98)	887	93 (89–97)
1979–1983	692	95 (91–100)	655	93 (88–99)	26	<i>80 (65–97)</i>	475	89 (84–95)	886	94 (90–98)
1984–1988	536	94 (89–99)	639	92 (87–98)	23	<i>91 (74–112)</i>	462	91 (86–96)	756	91 (87–95)
1989–1993	525	94 (89–100)	557	92 (87–98)	16	<i>91 (74–112)</i>	392	95 (89–101)	663	93 (89–97)
1994–1998	441	93 (88–98)	512	86 (81–92)	11	*	296	94 (88–101)	597	92 (88–96)
1999–2003	280	89 (84–94)	381	91 (87–95)	12	*	249	91 (86–97)	488	91 (88–95)
Women										
1964–1968	64	89 (76–104)	59	74 (60–91)	2	*	34	<i>99 (87–113)</i>	88	88 (78–99)
1969–1973	62	105 (96–116)	81	92 (82–104)	2	*	29	<i>99 (87–113)</i>	80	98 (87–109)
1974–1978	88	90 (79–103)	96	84 (74–94)	4	*	35	100 (86–116)	103	84 (74–96)
1979–1983	89	76 (66–87)	134	95 (88–104)	3	*	55	95 (84–108)	141	85 (77–94)
1984–1988	70	91 (79–104)	174	95 (89–101)	4	*	75	81 (71–93)	189	94 (88–100)
1989–1993	101	95 (86–105)	184	90 (82–98)	2	*	107	89 (80–98)	192	91 (85–98)
1994–1998	115	91 (83–101)	220	95 (89–101)	3	*	100	91 (82–102)	242	91 (86–97)
1999–2003	113	87 (81–95)	199	97 (92–101)	4	*	82	94 (87–101)	283	94 (90–98)

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. [6].

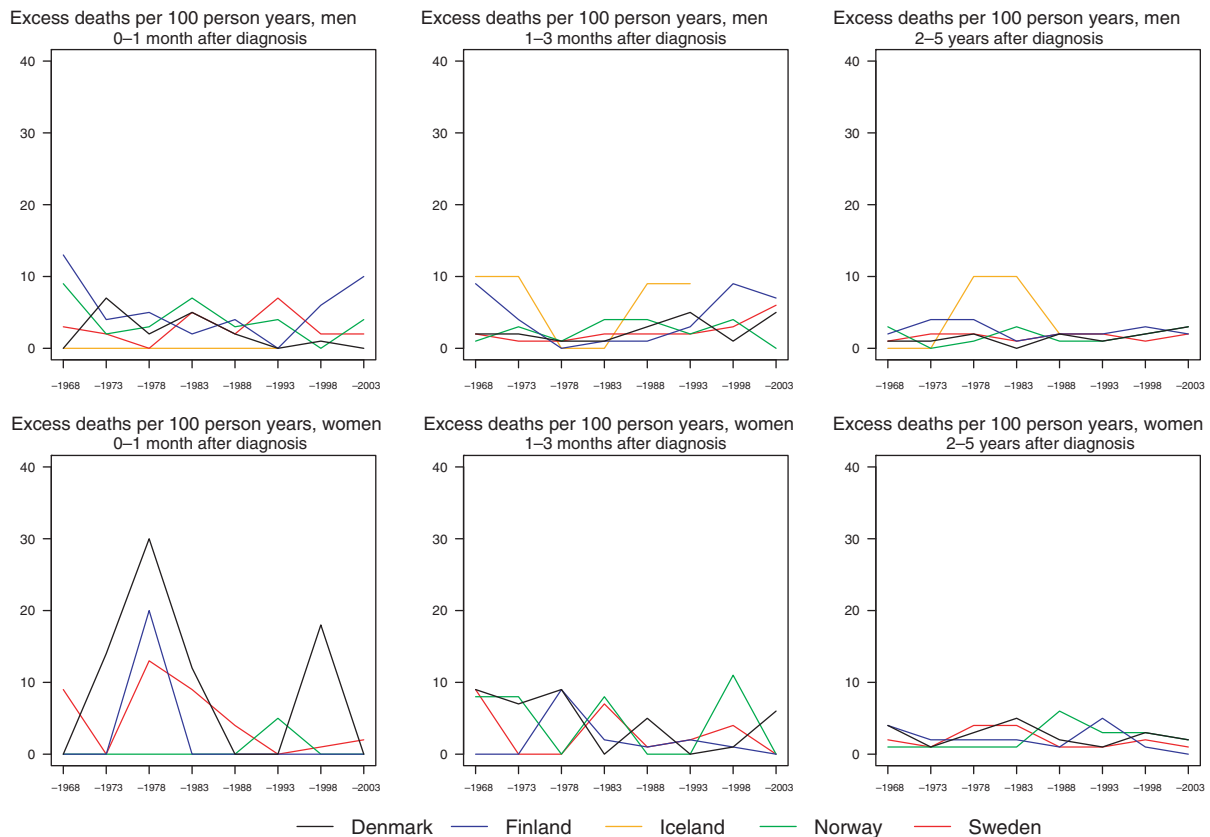


Figure 2. Trends in age-standardised (ICSS) excess death rates per 100 person years for lip cancer by sex, country, and time since diagnosis in Nordic cancer survival study 1964–2003.

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

Age	Men						Women					
	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	95	96	92	92	106	101	<i>103</i>	<i>103</i>	81	85	84	*
1969–1973	97	99	100	92	85	130	<i>103</i>	<i>103</i>	110	84	144	*
1974–1978	102	100	92	91	95	*	92	92	90	76	115	*
1979–1983	95	100	91	101	86	39	93	93	91	64	39	*
1984–1988	100	103	87	94	90	109	95	95	86	91	89	*
1989–1993	97	98	88	89	108	171	97	97	99	91	92	*
1994–1998	94	96	100	90	80	0	87	87	95	102	73	*
1999–2003	91	95	96	86	74	13	96	96	80	93	73	139
Finland												
1964–1968	93	86	87	79	77	*	78	78	88	68	51	*
1969–1973	91	91	84	77	78	*	96	96	82	107	75	*
1974–1978	96	92	85	79	73	*	<i>104</i>	<i>104</i>	82	66	82	*
1979–1983	91	90	91	100	91	*	99	99	98	90	96	*
1984–1988	91	88	99	93	85	51	<i>103</i>	<i>103</i>	103	89	74	131
1989–1993	86	92	91	86	110	92	88	88	105	94	57	54
1994–1998	86	86	96	88	68	0	98	98	104	91	79	0
1999–2003	95	91	94	88	86	43	97	97	104	94	88	144
Iceland												
1964–1968	93	93	93	<i>100</i>	67	*	*	*	*	*	*	*
1969–1973	93	93	93	<i>100</i>	67	*	*	*	*	*	*	*
1974–1978	81	81	81	88	60	*	*	*	*	*	*	*
1979–1983	81	81	81	88	60	*	*	*	*	*	*	*
1984–1988	87	87	87	<i>100</i>	90	*	*	*	*	*	*	*
1989–1993	87	87	87	<i>100</i>	90	*	*	*	*	*	*	*
1994–1998	<i>107</i>	<i>107</i>	<i>107</i>	*	54	*	*	*	*	*	*	*
1999–2003	<i>107</i>	<i>107</i>	<i>107</i>	*	54	*	*	*	*	*	*	*
Norway												
1964–1968	100	93	93	88	62	72	<i>102</i>	<i>102</i>	98	94	<i>105</i>	*
1969–1973	97	94	93	94	107	78	<i>102</i>	<i>102</i>	98	94	<i>105</i>	*
1974–1978	100	90	95	97	77	*	<i>102</i>	<i>102</i>	90	105	106	*
1979–1983	98	95	89	93	69	63	<i>102</i>	<i>102</i>	97	100	72	*
1984–1988	94	96	99	86	76	68	<i>101</i>	<i>101</i>	85	68	61	60
1989–1993	88	94	99	91	102	*	93	93	93	90	70	*
1994–1998	97	94	90	83	121	80	93	93	84	104	77	79
1999–2003	91	88	93	83	106	17	95	95	94	102	75	106
Sweden												
1964–1968	95	95	97	99	86	128	<i>103</i>	103	90	89	52	*
1969–1973	96	97	93	90	94	0	90	90	95	110	96	*
1974–1978	98	101	93	90	85	127	96	96	69	89	79	*
1979–1983	94	97	91	98	91	62	96	96	90	83	61	87
1984–1988	102	95	98	91	67	96	93	93	104	91	81	45
1989–1993	102	91	96	91	86	142	96	96	89	90	90	35
1994–1998	98	95	95	91	79	110	98	98	92	91	78	103
1999–2003	99	94	86	91	90	39	98	98	94	92	89	97

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. [6].

expected survival. Age-standardisation used the weights of the International Cancer Survival Standard (ICSS) cancer patient populations [7]. We present age-standardised (World) incidence and mortality rates, 5-year relative survival, and excess mortality rates for the follow-up periods of within one month,

1–3 months and 2–5 years following diagnosis, as well as age-specific 5-year relative survival by country, sex and 5-year period. Except for lip cancer, age-specific 5-year relative survival is not shown for the Icelandic patients because of the small number of patients involved.

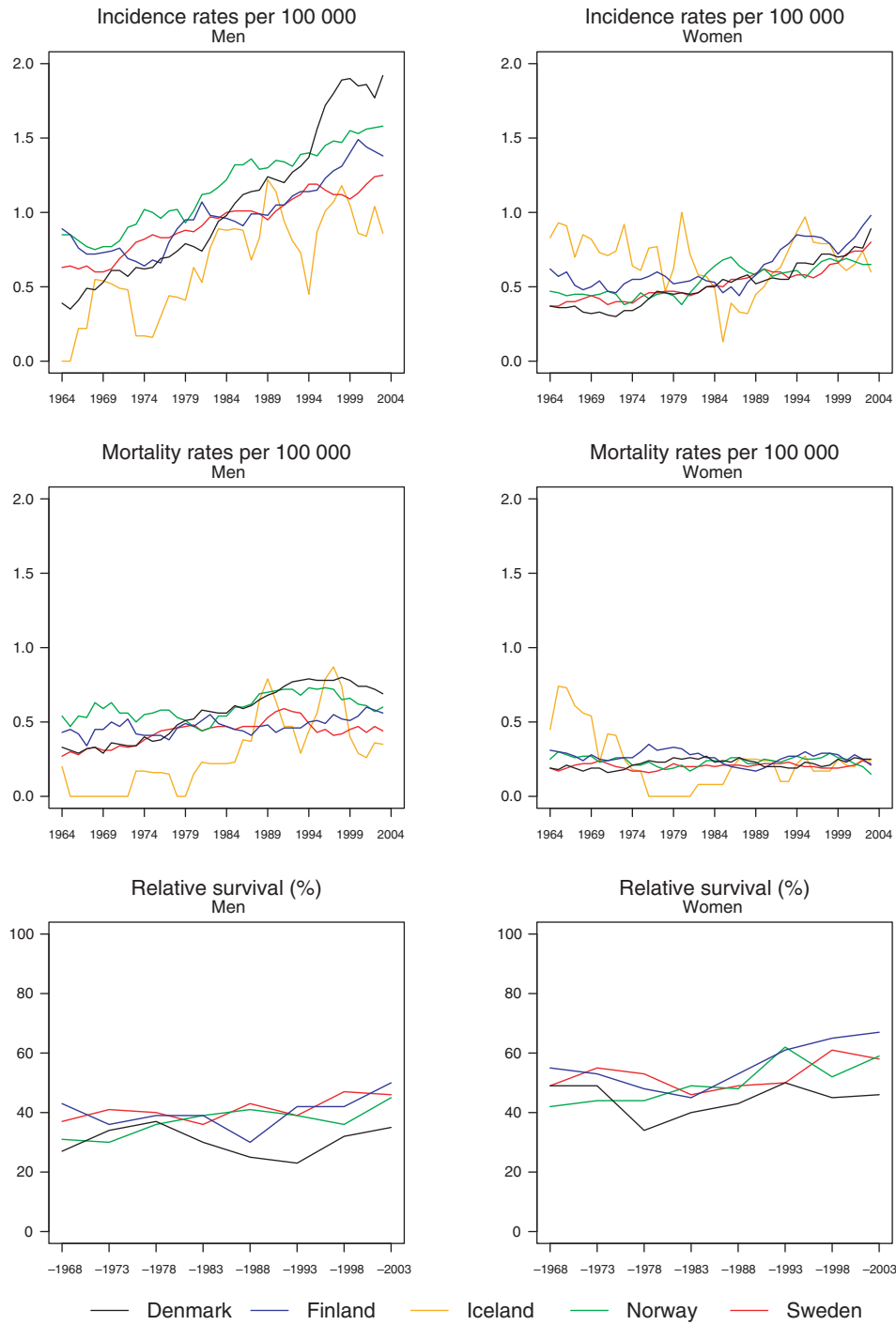


Figure 3. Trends in age-standardised (World) incidence and mortality rates per 100 000 and age-standardised (ICSS) 5-year relative survival for cancer of the tongue by sex and country. Nordic cancer survival study 1964–2003.

Results

Cancer of the lip

Incidence and mortality. The age-standardised incidence of lip cancer in males has been in a marked and steady decline in all the Nordic countries for decades (Figure 1). In 1999–2003, the observed decrease in Iceland appeared to cease, but this

may also be due to the inherent random variation. In 2003, the incidence rates were all between 1.0 and 1.6 per 100 000, the lowest in Sweden and the highest in Finland. At the beginning of the observation period, the incidence rates in females were considerably lower than those in males but, with declining rates in males and slightly increasing rates in females, the rates are approaching each other.

Table III. Trends in survival for cancer of the tongue 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	68	27 (18–42)	85	43 (28–66)	1	*	106	31 (23–43)	183	37 (29–46)
1969–1973	102	34 (23–49)	90	36 (23–56)	3	*	111	30 (22–42)	210	41 (33–51)
1974–1978	116	37 (26–52)	84	39 (30–52)	2	*	132	36 (26–48)	261	40 (32–50)
1979–1983	130	30 (21–43)	149	39 (30–52)	4	*	165	39 (30–50)	297	36 (29–45)
1984–1988	188	25 (19–33)	132	30 (22–40)	5	*	190	41 (33–52)	318	43 (35–51)
1989–1993	212	23 (16–32)	166	42 (34–53)	7	*	186	39 (30–51)	338	39 (33–46)
1994–1998	313	32 (25–40)	218	42 (34–52)	9	*	224	36 (30–44)	390	47 (41–54)
1999–2003	363	35 (30–40)	274	50 (42–59)	8	*	244	45 (39–51)	423	46 (41–51)
Women										
1964–1968	68	49 (40–60)	96	55 (43–69)	6	*	75	42 (31–58)	150	49 (40–60)
1969–1973	71	49 (40–60)	80	53 (40–71)	5	*	88	44 (33–58)	155	55 (46–65)
1974–1978	90	34 (25–46)	108	48 (39–60)	5	*	85	44 (33–59)	201	53 (46–62)
1979–1983	109	40 (30–52)	113	45 (36–56)	5	*	90	49 (38–64)	193	46 (38–55)
1984–1988	122	43 (33–54)	122	53 (44–65)	4	*	135	48 (39–58)	231	49 (41–57)
1989–1993	127	50 (40–61)	157	61 (52–71)	6	*	107	62 (52–74)	247	50 (44–58)
1994–1998	148	45 (37–55)	194	65 (57–74)	8	*	117	52 (42–63)	236	61 (54–68)
1999–2003	187	46 (40–53)	214	67 (61–74)	8	*	142	59 (51–67)	307	58 (53–64)

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. [6].

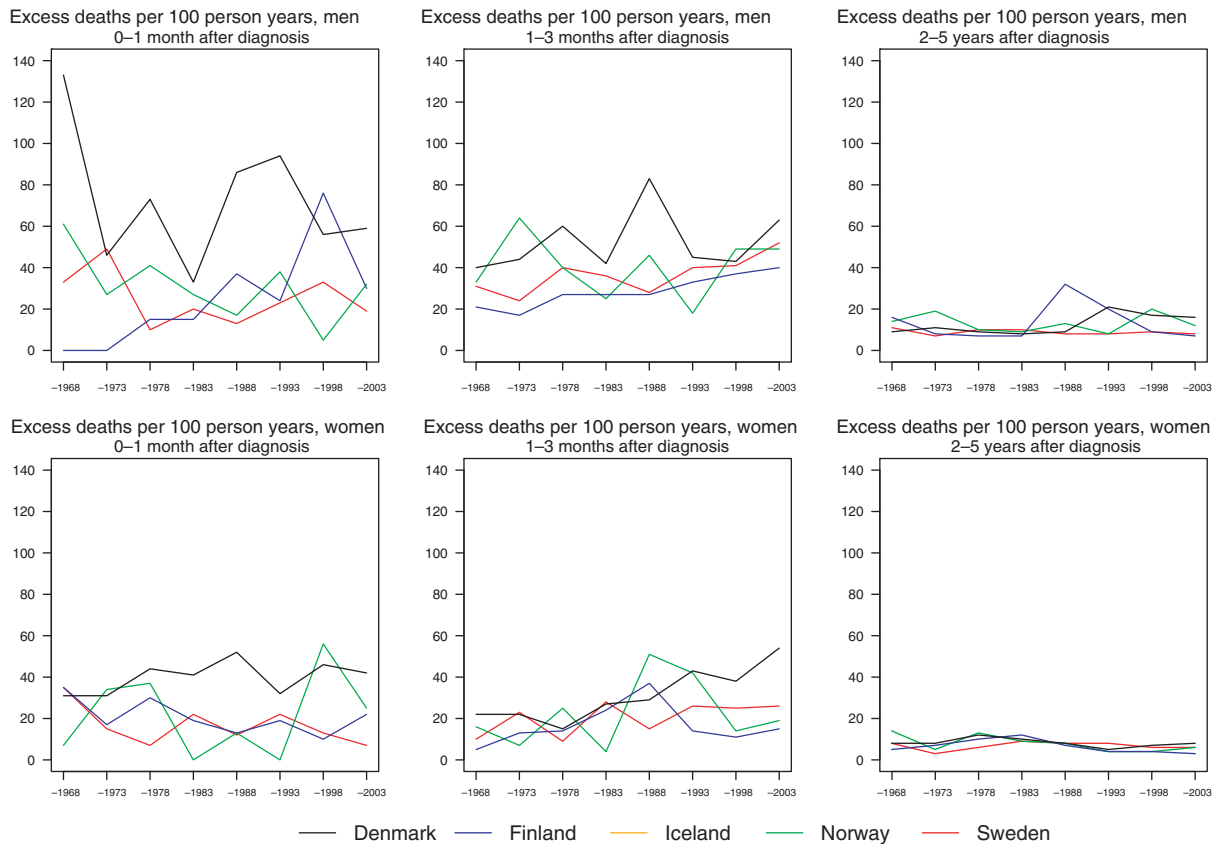


Figure 4. Trends in age-standardised (ICSS) excess death rates per 100 person years for cancer of the tongue by sex, country, and time since diagnosis in Nordic cancer survival study 1964–2003. No Icelandic curves. Too few patients to calculate rates for Iceland.

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

Age	Men						Women					
	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	21	38	40	27	0	*	68	62	47	45	32	*
1969–1973	44	43	27	32	30	*	68	62	47	45	32	*
1974–1978	48	32	45	32	30	*	43	49	50	17	14	*
1979–1983	27	35	28	24	41	*	45	30	54	29	40	*
1984–1988	48	33	22	27	0	*	42	52	33	54	29	*
1989–1993	33	30	17	21	19	*	42	49	56	49	45	*
1994–1998	50	41	26	27	25	*	76	48	38	44	33	*
1999–2003	54	46	29	37	13	*	79	53	47	36	29	0
Finland												
1964–1968	58	38	47	14	85	*	72	50	71	45	35	*
1969–1973	45	37	12	52	41	*	76	49	36	42	94	*
1974–1978	40	36	52	27	44	*	58	52	64	47	11	*
1979–1983	40	36	52	27	44	*	74	47	36	56	11	*
1984–1988	59	35	41	21	0	*	84	51	61	44	36	0
1989–1993	61	44	47	51	0	*	74	83	65	46	47	64
1994–1998	57	59	31	45	23	*	76	66	68	67	43	0
1999–2003	56	54	56	41	48	*	74	70	79	64	42	0
Norway												
1964–1968	68	50	25	18	16	*	58	58	51	16	48	*
1969–1973	43	50	34	15	20	*	51	51	64	32	19	*
1974–1978	46	48	37	30	23	*	47	47	54	50	8	*
1979–1983	55	36	35	44	24	*	46	46	40	54	62	0
1984–1988	68	47	35	43	22	*	60	60	51	39	34	*
1989–1993	59	37	40	31	40	*	69	69	73	49	55	188
1994–1998	47	49	48	32	0	*	67	67	53	46	30	0
1999–2003	55	59	51	41	16	*	72	72	62	58	30	24
Sweden												
1964–1968	72	45	33	33	12	*	63	62	38	47	47	*
1969–1973	64	43	28	45	35	*	90	59	62	38	42	*
1974–1978	41	35	45	30	53	*	62	65	63	47	27	*
1979–1983	61	33	38	25	40	*	72	47	36	40	54	0
1984–1988	47	50	37	36	53	*	69	46	55	45	32	89
1989–1993	62	45	31	39	28	*	62	71	57	34	36	0
1994–1998	67	49	48	32	57	*	73	69	73	53	34	90
1999–2003	71	50	46	36	40	*	77	64	62	53	36	54

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. [6]. Iceland not shown for the same reason.

Mortality from lip cancer is quite minimal (Figure 1); the average annual number of deaths in the Nordic countries in 1999–2003 due to this cancer being 17 and six in males and females, respectively. The mortality rates in males have decreased in the Nordic countries and appear to be approaching zero. In females, mortality rates have been consistently close to zero, on account of the rarity of the disease and the good prognosis of patients.

Survival. The age-standardised 5-year relative survival ratios have been between 90% and 100% (Figure 1, Table I). Due to limited numbers the

Icelandic female ratio could not be evaluated, and the figures presented for males are affected by random variation.

In males, the excess death rates were higher in the first follow-up month than in the subsequent periods of follow-up (Figure 2). There were no systematic inter-country differences. There was a tendency to observe somewhat poorer relative survival in patients aged 70 years or more (Table II). Some of the rates are higher than 100% due to zero observed deaths in the patient groups. This can result by chance where excess mortality is small or non-existent and the patient groups are small.

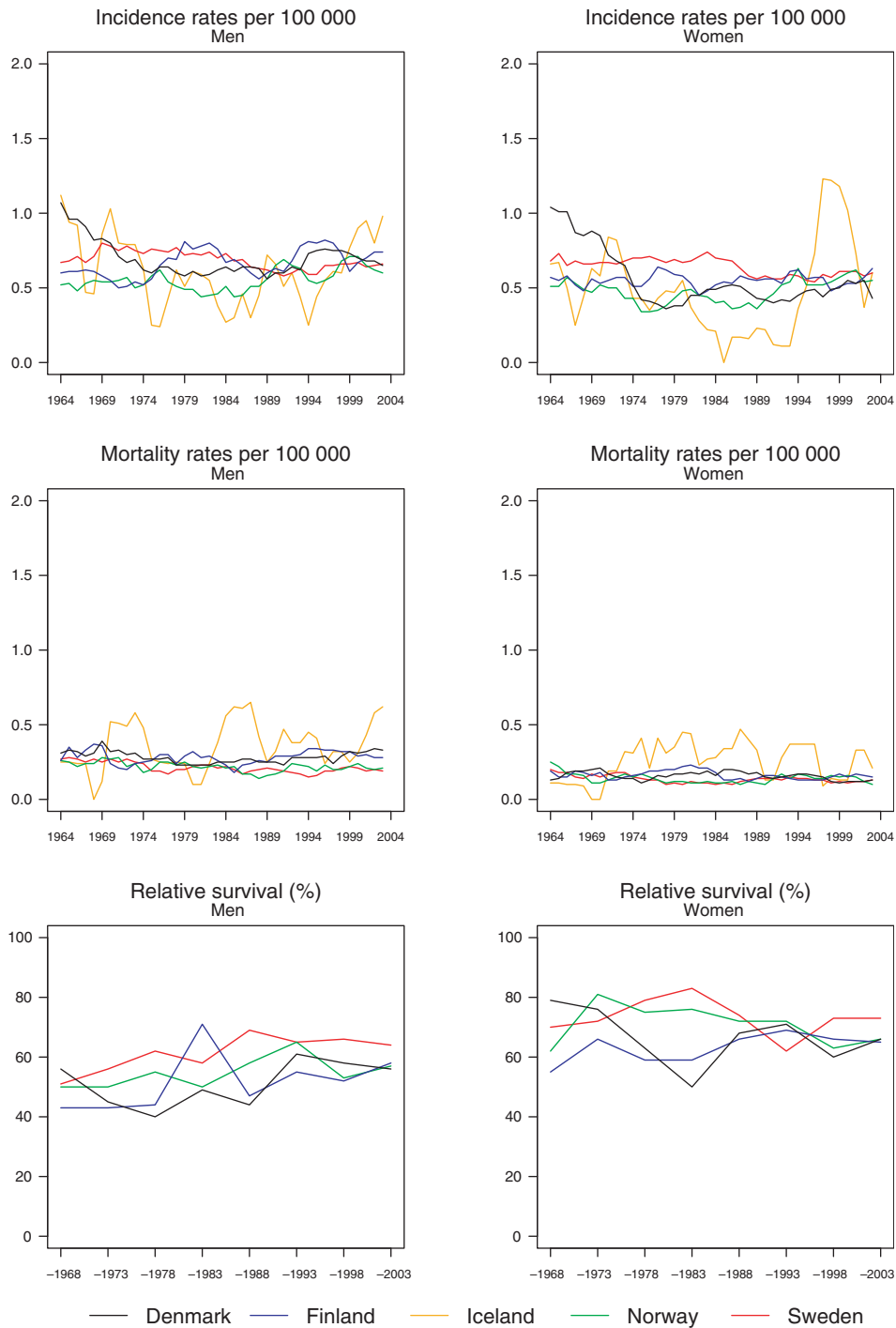


Figure 5. Trends in age-standardised (World) incidence and mortality rates per 100 000 and age-standardised (ICSS) 5-year relative survival for cancer of the salivary glands by sex and country. Nordic cancer survival study 1964–2003.

Cancer of the tongue

Incidence and mortality. The incidence has increased quite rapidly in males during the entire period (Figure 3). During the last decade, the Danish rates have accelerated to a level much higher than those in the other countries. The Icelandic rates have been consistently

the lowest among men in the Nordic countries, where age-standardised incidence rates range from 0.8 (Iceland) to 1.9 per 100 000 (Denmark) during the period 1999–2003. In females, there is very little variation between the countries during the most recent two decades, although the Finnish rates have had a tendency of being higher than those in the other countries.

Table V. Trends in survival for cancer of the salivary glands 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	139	56 (46–68)	63	43 (33–58)	4	*	60	<i>50 (41–62)</i>	190	51 (43–60)
1969–1973	115	45 (36–56)	59	43 (33–58)	4	*	71	<i>50 (41–62)</i>	215	56 (48–66)
1974–1978	109	40 (31–53)	84	44 (33–58)	2	*	82	55 (44–69)	226	62 (53–71)
1979–1983	103	49 (38–63)	105	71 (58–88)	4	*	64	50 (37–67)	235	58 (50–67)
1984–1988	119	44 (35–56)	96	47 (37–60)	3	*	69	58 (44–77)	231	69 (61–78)
1989–1993	112	61 (49–75)	97	55 (42–71)	4	*	108	65 (53–80)	206	65 (56–75)
1994–1998	149	58 (49–70)	145	52 (42–63)	5	*	90	53 (42–66)	232	66 (59–74)
1999–2003	142	56 (48–66)	128	58 (49–68)	9	*	110	57 (49–66)	246	64 (58–70)
Women										
1964–1968	163	79 (68–92)	84	55 (43–71)	2	*	79	62 (51–74)	178	70 (60–82)
1969–1973	125	76 (66–87)	84	66 (54–79)	5	*	71	81 (68–96)	212	72 (64–81)
1974–1978	75	63 (45–89)	96	59 (46–74)	2	*	57	75 (61–94)	236	79 (72–87)
1979–1983	96	50 (40–63)	98	59 (50–70)	4	*	75	76 (65–90)	229	83 (75–91)
1984–1988	111	68 (58–81)	111	66 (56–77)	1	*	60	72 (62–84)	235	74 (67–81)
1989–1993	84	71 (58–86)	121	69 (59–80)	2	*	74	72 (62–84)	213	62 (55–71)
1994–1998	113	60 (51–72)	118	66 (56–78)	5	*	93	63 (53–75)	210	73 (66–82)
1999–2003	126	66 (58–76)	133	65 (58–74)	6	*	107	66 (57–76)	238	73 (67–79)

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. [6].

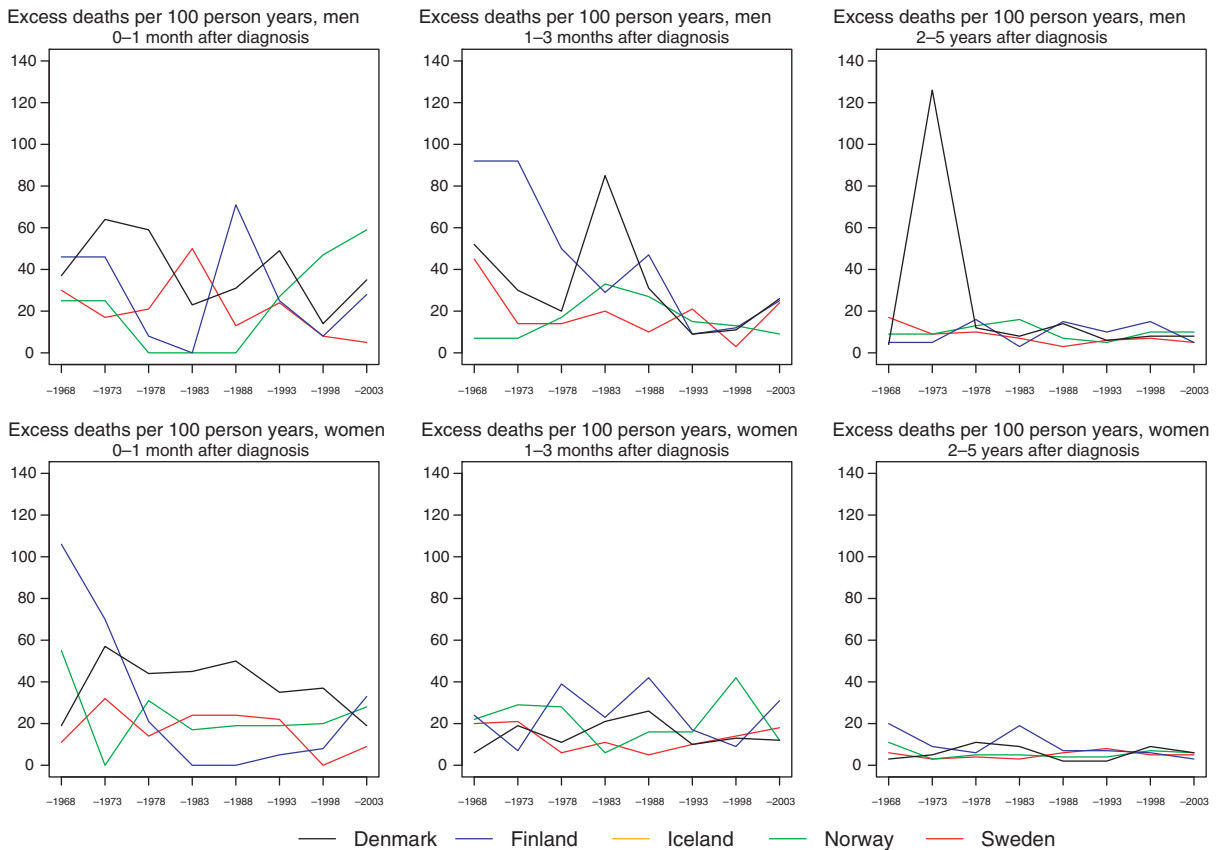


Figure 6. Trends in age-standardised (ICSS) excess death rates per 100 person years for cancer of the salivary glands by sex, country, and time since diagnosis in Nordic cancer survival study 1964–2003. No Icelandic curves. Too few patients to calculate rates for Iceland.

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

Age	Men						Women					
	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	86	71	53	54	21	*	97	85	80	70	72	*
1969–1973	51	71	56	40	0	*	90	99	88	69	28	*
1974–1978	77	35	48	34	15	*	63	85	44	61	77	*
1979–1983	66	41	57	46	34	*	90	67	51	42	15	*
1984–1988	81	55	30	46	23	*	81	56	68	78	53	*
1989–1993	75	60	59	73	29	64	95	83	60	79	41	*
1994–1998	94	71	51	53	40	*	96	84	55	45	44	*
1999–2003	87	72	44	42	63	*	91	76	66	60	50	*
Finland												
1964–1968	70	68	49	35	0	*	72	55	77	56	0	*
1969–1973	70	68	49	35	0	*	90	76	53	95	0	*
1974–1978	65	67	37	50	0	*	87	69	50	50	55	*
1979–1983	71	85	87	67	38	*	79	66	63	73	0	*
1984–1988	72	59	62	41	0	*	97	68	76	61	27	*
1989–1993	73	47	64	50	41	*	88	86	78	62	32	*
1994–1998	83	49	54	59	12	*	92	102	68	42	47	*
1999–2003	83	62	57	50	51	*	85	80	84	45	37	*
Norway												
1964–1968	80	61	53	45	19	*	95	69	78	61	0	*
1969–1973	80	61	53	45	19	*	90	84	85	88	48	*
1974–1978	85	69	44	74	0	*	82	51	79	77	88	*
1979–1983	80	93	41	19	52	*	96	73	91	73	44	*
1984–1988	84	71	61	46	41	*	90	75	74	74	48	*
1989–1993	80	70	67	53	69	*	90	75	74	74	48	*
1994–1998	79	72	39	62	17	*	90	92	62	59	20	*
1999–2003	87	86	56	44	27	*	92	77	69	61	37	*
Sweden												
1964–1968	87	54	58	55	0	*	90	85	79	55	53	*
1969–1973	93	67	59	51	20	*	90	78	73	71	52	*
1974–1978	84	69	59	69	26	*	97	87	90	72	53	*
1979–1983	86	63	69	43	38	*	90	89	81	78	82	*
1984–1988	84	72	71	66	57	*	89	89	83	69	37	*
1989–1993	91	60	72	55	56	0	91	74	57	64	32	0
1994–1998	80	76	65	73	32	94	90	84	75	59	73	56
1999–2003	75	71	71	60	39	*	95	72	81	61	63	39

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. [6]. Iceland not shown for the same reason.

In Iceland, the rates before 1980 were systematically higher in females than in males but the underlying numbers are small. The mortality rates show a much more modest increase in Danish males than seen in the incidence rates, while in the Norwegian trends, the mortality decrease apparent in men during 1994–2003, was not observed for incidence (Figure 3).

Survival. The age-standardised 5-year relative survival ratios in Denmark have during the three last decades been below those observed in the other Nordic countries (Figure 3, Table III). Female patients tend to have higher survival compared to men, while the increases in survival over time also appear more rapid in females than in males.

Danish patients tend to have higher excess death rates during the first three months than the patients in the other countries (Figure 4). The excess death rates have stayed fairly constant over time during the first year of follow-up (data not shown for 3–12 months of follow-up). In the subsequent years of follow-up, rates have been lower. There is a tendency towards decreasing survival with advancing age at diagnosis (Table IV).

Cancer of the salivary glands

Incidence and mortality. The incidence rates in both sexes have stayed fairly constant over time in the last two decades, and there has been very little

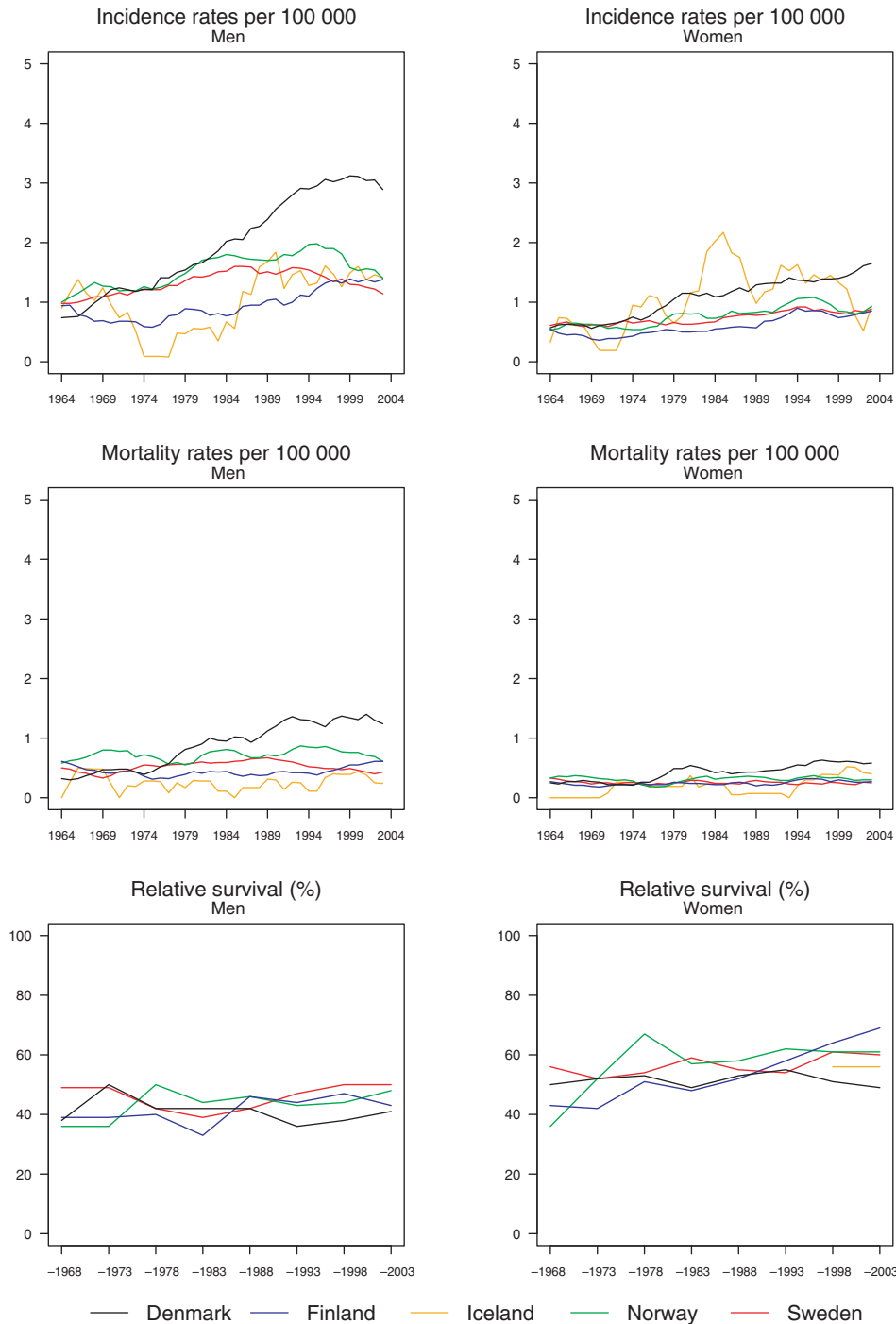


Figure 7. Trends in age-standardised (World) incidence and mortality rates per 100 000 and age-standardised (ICSS) 5-year relative survival for cancer of the mouth by sex and country. Nordic cancer survival study 1964–2003.

variation between countries (Figure 5). The age-standardised incidence rates have been around 0.6 per 100 000 in males and 0.5 in females. Before 1980, a steep decline occurred in the rates in Denmark. The mortality rates conveyed a slightly decreasing trend with little systematic variation between countries, particularly among females (Figure 5).

Survival. In males, the Swedish age-standardised 5-year relative survival ratios are somewhat higher than those in the other Nordic countries over the last two decades (Figure 5, Table V). There seems to be a slight upward tendency in the ratios in males, but overall they still have remained lower than those of females. The small frequencies in Iceland do not permit calculation of relative survival.

Table VII. Trends in survival for cancer of the mouth 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	123	38 (29–50)	84	39 (28–53)	6	*	153	36 (28–46)	302	49 (42–57)
1969–1973	209	50 (41–60)	81	39 (28–53)	4	*	174	36 (28–47)	368	49 (44–55)
1974–1978	249	42 (35–51)	79	40 (29–54)	1	*	185	50 (42–60)	401	42 (37–49)
1979–1983	298	42 (35–51)	116	33 (25–44)	5	*	254	44 (37–52)	475	39 (34–45)
1984–1988	361	42 (35–51)	137	46 (35–59)	9	*	259	46 (39–54)	525	42 (37–48)
1989–1993	482	36 (30–42)	152	44 (35–56)	10	*	280	43 (36–50)	518	47 (41–52)
1994–1998	567	38 (33–45)	233	47 (38–57)	12	*	290	44 (38–52)	502	50 (45–55)
1999–2003	604	41 (36–46)	265	43 (38–49)	13	*	250	48 (42–55)	478	50 (46–54)
Women										
1964–1968	120	50 (40–62)	70	43 (33–56)	4	*	104	36 (26–48)	237	56 (49–64)
1969–1973	130	52 (43–63)	67	42 (31–56)	1	*	97	52 (42–65)	219	52 (46–60)
1974–1978	180	53 (45–63)	97	51 (41–63)	10	*	107	67 (57–80)	273	54 (48–62)
1979–1983	284	49 (42–56)	107	48 (39–59)	9	*	154	57 (49–67)	282	59 (53–66)
1984–1988	283	53 (47–60)	131	52 (43–63)	15	*	185	58 (51–66)	340	55 (49–61)
1989–1993	308	55 (49–62)	177	58 (50–68)	10	*	177	62 (54–72)	380	54 (48–60)
1994–1998	345	51 (45–57)	219	64 (57–72)	19	56 (40–79)	222	61 (54–70)	403	61 (56–67)
1999–2003	377	49 (44–54)	210	69 (63–75)	12	56 (40–79)	181	61 (55–68)	414	60 (56–64)

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. [6].

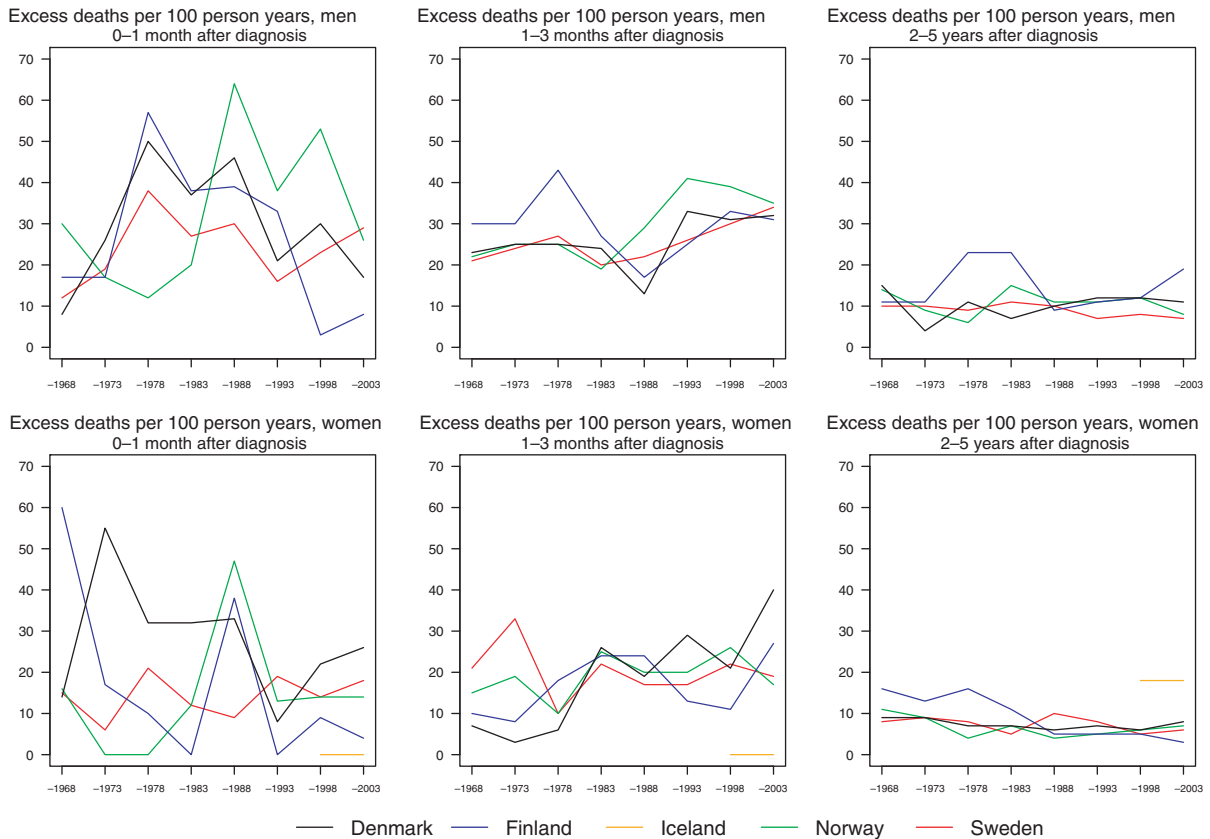


Figure 8. Trends in age-standardised (ICSS) excess death rates per 100 person years for cancer of the mouth by sex, country, and time since diagnosis in Nordic cancer survival study 1964–2003.

Table VIII. Trends in 5-year age-specific relative survival in percent after cancer of the mouth by sex and country. Nordic cancer survival study 1964–2003.

Age	Men						Women					
	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	32	47	36	49	13	*	82	61	53	38	31	*
1969–1973	71	55	43	51	36	*	47	69	71	45	18	*
1974–1978	44	46	43	43	32	*	58	66	58	52	29	*
1979–1983	48	44	39	32	62	*	67	64	40	44	40	73
1984–1988	53	36	39	37	58	0	73	68	48	48	36	0
1989–1993	42	41	38	29	33	0	85	57	59	45	43	0
1994–1998	54	43	35	40	22	0	80	59	53	45	24	0
1999–2003	50	39	36	45	37	0	77	48	56	40	31	0
Finland												
1964–1968	69	44	35	29	34	*	71	71	53	26	0	*
1969–1973	69	44	35	29	34	*	63	63	56	29	0	*
1974–1978	48	55	54	34	0	*	63	63	51	66	0	*
1979–1983	41	56	49	19	0	*	71	71	43	47	13	*
1984–1988	55	60	41	49	25	*	69	69	60	32	41	*
1989–1993	55	41	48	39	41	*	60	60	79	44	45	*
1994–1998	62	57	49	46	20	*	77	77	72	52	45	*
1999–2003	57	50	50	48	4	*	86	86	64	64	54	27
Norway												
1964–1968	73	55	28	13	44	0	71	47	28	21	37	*
1969–1973	46	35	38	33	34	*	81	69	61	41	19	*
1974–1978	66	44	60	43	42	*	84	80	54	68	64	*
1979–1983	49	56	40	50	21	0	76	77	54	54	33	45
1984–1988	73	48	49	44	19	0	94	80	64	43	24	47
1989–1993	71	54	41	34	26	*	62	74	64	64	42	0
1994–1998	75	55	36	37	35	*	70	61	60	61	60	0
1999–2003	64	53	37	50	46	*	64	74	58	59	53	16
Sweden												
1964–1968	60	51	54	35	53	*	82	70	62	39	45	*
1969–1973	73	67	47	52	9	*	101	76	51	33	26	*
1974–1978	63	39	47	39	29	0	76	74	55	42	37	46
1979–1983	59	38	46	35	18	0	83	68	67	55	27	0
1984–1988	52	44	48	36	32	0	82	60	63	47	29	24
1989–1993	52	57	43	42	46	171	70	65	57	47	36	26
1994–1998	70	58	50	42	39	63	70	76	64	52	51	51
1999–2003	79	55	56	37	33	49	74	75	61	51	47	20

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. [6]. Iceland not shown for the same reason.

There is a lot of random variation in the excess death rates, and no systematic differences between countries can be seen (Figure 6). The relative survival ratios are high in the youngest group, although they decline with advancing age at diagnosis (Table VI).

Cancer of the mouth

Incidence and mortality. Denmark has over time become the country with the highest incidence, with rates in men twice as high as those observed in the other Nordic countries (Figure 7). The temporal development has been quite heterogeneous in males between the countries. The increase in Denmark seems to have attenuated recently. In Norway and Sweden, the rates

have been decreasing over the period 1994–2003. In Finland, the development is similar to Denmark, although in absolute terms, rates are at a much lower level, while rates in Iceland have not been substantively altered over the last 20 years. Trends are similar in women, although the high incidence in Iceland is comparable to that among Danish women, with incidence and mortality rates similar between the sexes. The mortality rates display comparable patterns to the incidence rates but at a considerably lower level (Figure 7).

Survival. The Danish age-standardised 5-year relative survival ratios have during the most recent years not

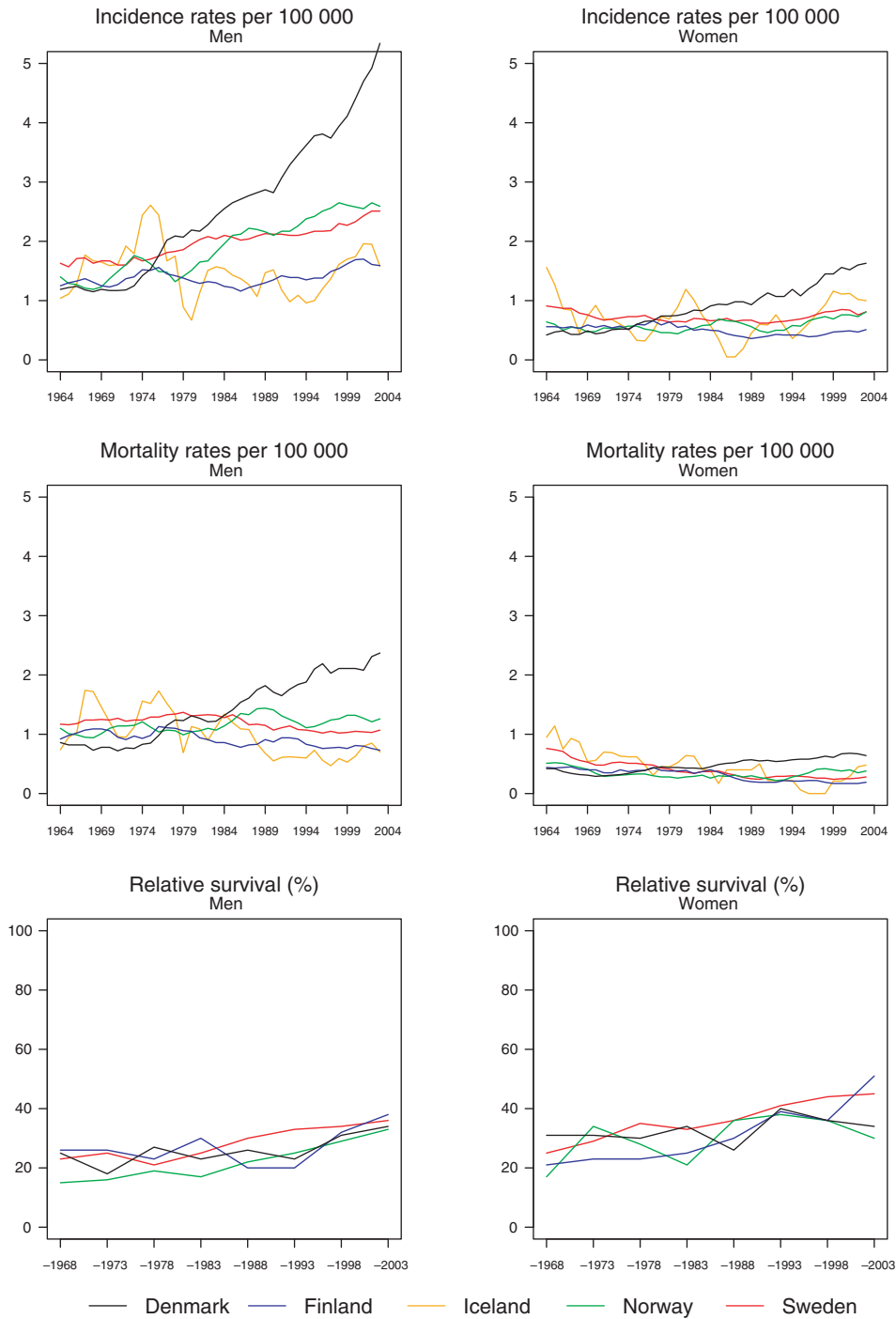


Figure 9. Trends in age-standardised (World) incidence and mortality rates per 100 000 and age-standardised (ICSS) 5-year relative survival for pharyngeal cancer by sex and country. Nordic cancer survival study 1964–2003.

shown the increasing trends observed in the ratios for Finland, Norway and Sweden (Figure 7, Table VII). Overall, the ratios in females have tended to increase more rapidly with time than those for males.

The excess death rates of the patients have by and large decreased in the first month (although there is a large degree of random variation) and in females 2–5 years after diagnosis in addition (Figure 8). There is no discernible decline in excess mortality during the

second and third month after diagnosis. There is however a tendency for relative survival to decrease with advancing age at diagnosis (Table VIII).

Cancer of the pharynx

Incidence and mortality. The incidence has increased sharply in Denmark, and to a lesser extent in Norway and Sweden, while rates are reasonably stable in

Table IX. Trends in survival for pharyngeal cancer 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	190	25 (19–33)	145	26 (12–54)	6	*	164	15 (10–21)	489	23 (19–28)
1969–1973	192	18 (13–25)	152	26 (15–46)	10	*	206	16 (12–22)	483	25 (20–31)
1974–1978	301	27 (21–34)	196	23 (17–30)	14	*	213	19 (14–25)	552	21 (17–25)
1979–1983	373	23 (19–29)	176	30 (23–41)	9	*	243	17 (13–23)	644	25 (21–30)
1984–1988	475	26 (21–33)	174	20 (15–28)	9	*	299	22 (17–31)	666	30 (26–34)
1989–1993	528	23 (19–28)	219	20 (15–27)	9	*	308	25 (20–33)	697	33 (29–37)
1994–1998	693	31 (26–37)	238	32 (24–42)	9	*	369	29 (25–35)	707	34 (30–38)
1999–2003	907	34 (30–38)	329	38 (33–44)	16	*	392	33 (29–37)	831	36 (34–39)
Women										
1964–1968	88	31 (22–44)	84	21 (13–35)	4	*	76	17 (11–29)	283	25 (21–31)
1969–1973	80	31 (22–45)	96	23 (14–36)	4	*	80	34 (24–50)	245	29 (23–36)
1974–1978	122	30 (21–42)	110	23 (16–32)	2	*	86	28 (20–39)	280	35 (30–41)
1979–1983	157	34 (27–42)	115	25 (18–36)	7	*	89	21 (14–32)	240	33 (27–39)
1984–1988	175	26 (21–34)	90	30 (21–41)	1	*	104	36 (27–49)	258	36 (30–43)
1989–1993	224	40 (33–48)	94	39 (30–51)	4	*	79	38 (29–49)	238	41 (35–48)
1994–1998	252	36 (30–44)	89	36 (27–49)	5	*	112	36 (27–47)	266	44 (38–50)
1999–2003	308	34 (29–39)	108	51 (43–61)	10	*	136	30 (25–36)	299	45 (41–50)

*Too few patients to calculate survival, see ref. [6].

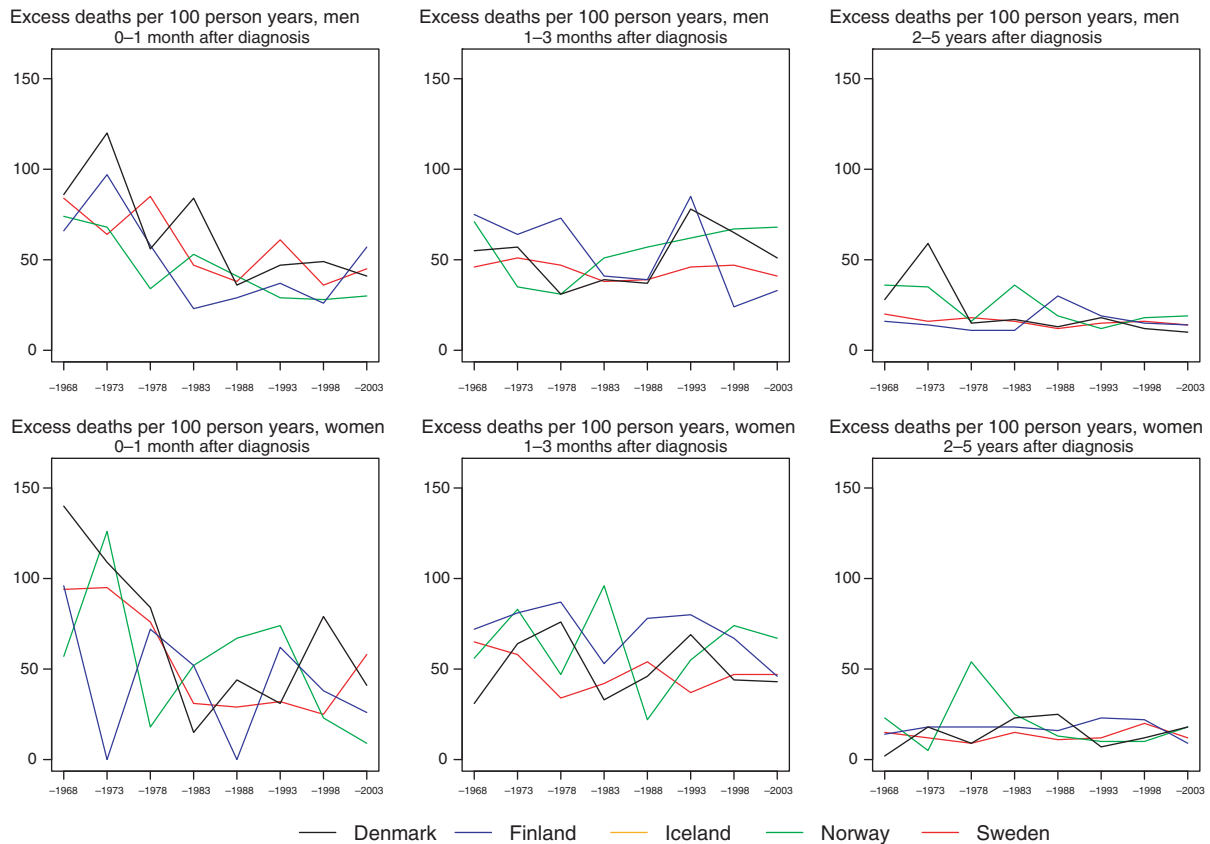


Figure 10. Trends in age-standardised (ICSS) excess death rates per 100 person years for pharyngeal cancer by sex, country, and time since diagnosis in Nordic cancer survival study 1964–2003. No Icelandic curves. Too few patients to calculate rates for Iceland.

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

Age	Men						Women					
	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	41	27	31	26	0	*	28	43	32	41	0	*
1969–1973	36	25	20	15	0	*	36	33	48	29	0	*
1974–1978	51	29	35	11	20	*	37	46	30	19	26	*
1979–1983	40	26	31	15	8	0	44	55	43	26	0	*
1984–1988	41	22	24	21	33	*	29	41	43	15	0	*
1989–1993	35	25	27	20	9	*	59	42	44	41	13	*
1994–1998	48	34	25	29	31	0	42	45	36	24	46	*
1999–2003	51	38	29	26	39	*	58	48	38	17	25	*
Finland												
1964–1968	33	16	23	10	67	*	29	24	21	15	23	*
1969–1973	26	18	25	21	47	*	37	17	26	9	38	*
1974–1978	45	40	14	24	0	*	56	28	21	20	0	*
1979–1983	44	41	23	33	18	*	53	19	22	28	11	*
1984–1988	51	18	26	13	0	*	65	40	21	26	14	*
1989–1993	46	28	16	17	0	*	60	60	44	34	0	*
1994–1998	59	48	28	19	23	*	50	42	35	47	0	*
1999–2003	63	51	38	37	7	*	75	63	59	43	22	*
Norway												
1964–1968	48	17	19	3	0	*	32	32	12	17	0	*
1969–1973	40	31	18	5	0	*	34	34	46	29	25	*
1974–1978	36	35	19	12	0	*	45	45	43	12	0	*
1979–1983	43	26	15	13	0	*	37	37	31	7	0	*
1984–1988	25	39	22	14	18	*	52	52	27	34	27	*
1989–1993	52	33	19	18	21	*	71	71	33	29	0	*
1994–1998	62	45	31	16	9	*	47	47	30	30	35	*
1999–2003	68	54	34	17	8	*	62	62	26	10	12	*
Sweden												
1964–1968	46	23	18	27	7	*	51	52	22	15	0	*
1969–1973	48	27	21	17	27	*	59	34	26	21	20	*
1974–1978	43	24	19	16	12	*	83	48	29	23	16	0
1979–1983	52	29	20	16	27	*	70	38	36	24	7	*
1984–1988	59	34	25	20	29	*	66	46	36	32	9	*
1989–1993	62	39	30	23	24	*	67	58	37	36	16	*
1994–1998	59	49	41	19	11	*	76	58	54	36	0	0
1999–2003	68	58	40	21	10	*	70	74	51	32	9	*

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. [6]. Iceland not shown for the same reason.

Iceland and Finland (Figure 9). The age-standardised incidence rates in 1999–2003 ranged in males from 1.7 in Finland and Iceland to 4.7 per 100 000 in Denmark. In females, rates range from 0.5 in Finland to 1.5 per 100 000 in Denmark. Mortality has been increasing only in Denmark, whereas rates have remained fairly stable during the last decades in the other countries (Figure 9).

Survival. The age-standardised relative survival ratios have been steadily increasing over time in both sexes (Figure 9, Table IX). The survival of female patients has been higher than that of male patients. The differ-

ences between the countries were fairly unsystematic but the ratios in Sweden have had a tendency to be slightly higher than the others. No ratios from Iceland can be reported due to the small numbers of cases.

The excess death rates of the patients have been the highest in the first month after diagnosis, where they have decreased markedly with time (Figure 10). No such decreases are observable in the other follow-up periods studied.

The relative survival tends to be highest among the youngest patients (Table X). There have been increments in survival in all age groups and countries, although in some age groups this cannot be documented because of the small number of cases.

Discussion

The survival of patients following a diagnosis of lip cancer is very high with a rather limited potential for further improvement in prognosis. There are few survival differences by country, sex, age, or time period. As well as solar radiation, smoking is a known risk factor for lip cancer and may cause some co-morbidity resulting in an excess risk of death among patients. The Icelandic figures should be interpreted with caution due to the extremely small numbers involved.

The improvement in tongue cancer survival has been rather modest. The recent incidence peak in Denmark is not apparent in the relative survival even though the latter has been obtained by the hybrid method yielding the most up-to-date results. Continued follow-up will reveal whether the increase in incidence is accompanied by an increase in relative survival in Denmark, given the less dramatic changes in mortality.

There has been very little improvement in relative survival of patients with cancer of the salivary glands with time, and the differences between countries are small. The trends may also be affected by coding practices; the clinical and morphological evaluation of mixed tumours (pleomorphic adenomas), their reporting and coding at the Finnish Cancer Registry have, for example, changed over time [8].

The stability of the relative survival ratios suggests that the increases in mouth and pharyngeal cancer incidence in Denmark are real and not primarily the result of differences in definitions or coding. The oral tumours form a heterogeneous group that may complicate comparisons. Smoking and alcohol are risk factors for oral cancers that may also have an effect on co-morbidity in a synergistic way, thus lowering the relative survival of the patients. Thus far, the higher consumption of oral tobacco in Sweden than in the other Nordic countries [9,10] is neither reflected in the incidence rates nor the relative survival ratios of the patients.

Many recent advances in therapy together with new standards of care [11] are likely to play an important role in the observed increases in relative survival also in the Nordic countries. Also of particular clinical importance is the prognostic significance of the role of the HPV infection in squamous cell carcinomas of the oropharynx [3]. The HPV-infected patients have a better prognosis than those not infected [12].

Overall, patient survival has improved moderately in the Nordic countries. A likely continuation of the improvement may be expected with better targeted therapies. A lowering of risk and co-morbidity via primary prevention strategies that reduce

the prevalence of smoking and alcohol in the Nordic populations presents a further challenge.

Acknowledgement

The Nordic Cancer Union (NCU) had 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, Klint Å, Ólafsdóttir E, et al. (2008). NORDCAN: Cancer incidence, mortality and prevalence in the Nordic countries, version 3.3. Association of Nordic Cancer Registries. Danish Cancer Society (<http://www.ancr.nu>). Accessed 24 April 2009.
- [2] Mayne ST, Morse DE, Winn DM. Cancers of the oral cavity and pharynx. In: Schottenfeld D, Fraumeni JF Jr, editors. *Cancer epidemiology and prevention*. 3rd ed. Oxford: Oxford University Press; 2006. pp. 674–96.
- [3] Fakhry C, Gillison ML. Clinical implications of human papillomavirus in head and neck cancers. *J Clin Oncol* 2006; 24:2606–11.
- [4] Berrino F, Capocaccia R, Coleman MP, Estève J, Gatta G, Hakulinen T, et al., editors. *Survival of cancer patients in Europe: the EURO-CARE-3 Study*. *Ann Oncol* 2003;14: Suppl 5.
- [5] Verdecchia A, Guzzinati S, Francisci S, De Angelis R, Bray F, Allemani C, et al. Survival trends in European cancer patients diagnosed in 1988 to 1999. *Eur J Cancer* 2009; 45:1042–66.
- [6] Engholm G, Gislum M, Bray F, Hakulinen T. Trends in the survival of patients diagnosed with cancer in the Nordic countries 1964–2003 and followed up to the end of 2006. Material and methods. *Acta Oncol* 2010;49:545–60
- [7] Corazziari I, Quinn M, Capocaccia R. Standard cancer patient population for age standardising survival ratios. *Eur J Cancer* 2004;40:2307–16.
- [8] Dickman PW, Hakulinen T, Luostarinen T, Pukkala E, Sankila R, Söderman B, et al. Survival of cancer patients in Finland 1955–1994. *Acta Oncol* 1999;38:Suppl. 12.
- [9] Dreyer L, Winther JF, Pukkala E, Andersen A. Tobacco smoking. In: Olsen JH, Andersen A, Dreyer L, Pukkala E, Tryggvadóttir L, Gerhardtsson de Verdier M, et al. *Avoidable cancers in the Nordic countries*. *APMIS* 1997;105:Suppl 76:9–47.
- [10] Brennan P, Mucci L, Adami HO. Oral and pharyngeal cancer. In: Adami HO, Hunter D, Trichopoulos D, editors. *Textbook of cancer epidemiology*. 2nd ed. Oxford: Oxford University Press; 2008. pp. 155–74.
- [11] Forastiere AA, Trotti A, Pfister DG, Grandis JR. Head and neck cancer: Recent advances and new standards of care. *J Clin Oncol* 2006;24:2603–5.
- [12] Fakhry C, Westra WH, Li S, Cmelak A, Ridge JA, Pinto H, et al. Improved survival of patients with human papillomavirus – positive head and neck squamous cell carcinoma in a prospective clinical trial. *J Natl Cancer Inst* 2008;100:261–9.