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Original Paper

Variation in Survival of Patients with Head and Neck Cancer in Europe by the Site of Origin of the Tumours

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The study describes the prognosis of head and neck cancer in Europe on the basis of information available to population-based cancer registries collaborating in the EUROCARE II project. Variation in survival in relation to country and the anatomical site/sub-site of origin of the tumours was examined. Survival analysis was carried out on 35 004 head and neck cancer cases (ICD 141, 143–148 and 161) diagnosed between 1985 and 1989 in 17 European countries. Prognosis varied considerably according to anatomical site: the best 5-year survival rates were seen for cancer of the larynx (63% in men) and the worst for cancer of the hypopharynx (22% in men). Five-year relative survival of male patients with cancer of the tongue, mouth and pharynx (ICD 141, 143–148) was 34% and ranged from over 45% in Iceland, Sweden, The Netherlands and Austria to less than 25% in Eastern European countries. Survival for larynx cancer ranged from over 70% in Iceland, Sweden, The Netherlands and Germany to less than 50% in Slovakia, Poland and Estonia. Apparently, France had the lowest survival (relative risk (RR) of dying versus Finland = 1.29) in Western Europe; after adjustment for ICD 3-digit anatomical sites the difference disappeared (RR = 1.04). Eastern European countries remained at the bottom of the survival range (RR > 1.4). The analyses adjusting by sub-site (ICD fourth digit) were confined to registries for which the proportion of unspecified sub-sites was less than 20%. Geographical differences in survival between Western European countries were largely due to a difference in case mix of anatomical sub-sites. However, after correcting for different sub-site distribution, differences persisted between Eastern and Western European countries. This is likely to be due to late diagnosis and to late referral or poor access of patients to adequately equipped treatment centres.

Key words: population-based cancer registries, relative survival, head and neck cancers, cancer, Cox proportional hazards, Europe, tongue, oral cavity, oropharynx, hypopharynx , larynx
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INTRODUCTION

HEAD AND neck cancers are the fourth most common cancer in men in the European Union [1], after cancer of the lung, colorectal and prostate cancers. The epidemiology is characterised by a strong incidence gradient, with rates increasing from Northern to Mediterranean countries; Eastern countries have shown intermediate incidence rates [2]. The highest incidence was registered in France, where it is as high as lung cancer (approximately 50/100 000 men-year, World standardised rate), the lowest in Sweden and U.K. (9 and 10 per 100 000, respectively). Such large geographical variability reflects a different prevalence of lifestyle risk factors, such as alcohol drinking, tobacco smoking, the type of tobacco [3] and dietary habits [4], which may have independent influence on prognosis [5]. The incidence of head and neck cancers in women is lower than in men (the overall annual age standardised incidence rate in the EU has been estimated at 26 per 100 000 in men and 3.1 per 100 000 women) [1] and the geographical pattern is quite different, with lower variability than in men but with fairly high rates (3–4/100 000) in France, Switzerland, Scotland and Denmark and lower rates in Spain and Southern Italy, Finland and Eastern Countries (around 2/100 000 or less).

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The anatomy of the upper respiratory and digestive tract is very complex for the non specialist. Even specialists use rather subjective criteria for the definition of the borders between contiguous organs and the oncological classifications for this anatomical region are not consistent. The base of the tongue, for instance, is classified with tongue in ICD-IX (International Classification of Diseases, ninth revision) [6] and with oropharynx in the UICC-TNM *Classification of Malignant Tumours* [7]. The classification of tumours arising at the border between larynx and pharynx, sometimes called epilarynx, is also inconsistent. According to the ICD, for instance, the anterior surface and free border of the epiglottis, as well as the carrefour between the epiglottic border, the ari-epiglottic and the pharyngo-epiglottic fold, belong to the oropharynx (ICD 146) and the border of the ari-epiglottic fold to the hypopharynx (ICD 148), but in TNM classification tumours arising in these sites are included in supraglottic laryngeal cancer. The term extrinsic larynx is still used, which sometimes refers to supraglottic larynx (ICD 161.1) and sometimes to lesions overlapping the larynx and pharynx which should be coded either to oro- or hypopharynx or to pharynx NOS (ICD 149).

There is ample clinical evidence that the site of origin of head and neck cancer is a major determinant of prognosis, both because of the different stage at diagnosis and because of the different possibilities of surgical treatment. The sub-site within the oral cavity, larynx and pharynx is also a major factor. Cancer of the base of tongue, for instance, has a worse prognosis than those arising in the rest of the oral cavity; cancer of the tonsil has a better prognosis than cancers arising in other parts of the oropharynx; supraglottic cancer has a worse prognosis than glottic cancer; and the prognosis of cancer arising in the epilarynx is worse than supraglottic but better than hypopharyngeal cancer [8–11].

Unfortunately, only a few registries have collected detailed information on the fourth digit sub-site of head and neck cancers. They are sufficient, however, to clarify that the case mix within 3-digit categories of head and neck cancers varies considerably between different European populations. As a general pattern Southern European countries tend to have a higher incidence of cancer of the pyriform sinus (particularly in France), supraglottic larynx (particularly in Spain) and the base of the tongue, which have a worse prognosis with respect to other sub-sites within the pharynx, larynx and oral cavity. Notable exceptions are Southern Italy (showing a lower incidence of all head and neck cancers and also a lower proportion of sub-sites with poor prognosis), British women (with a relatively high incidence of retrocricoid cancer, which also has a poor prognosis) and larynx cancer among women (characterised by a higher proportion of supraglottic sites in Northern and Central Europe and of glottic cancer in Mediterranean and Eastern countries) [12].

The aim of this study was to describe the prognosis of head and neck cancers in Europe on the basis of the information available to cancer registries collaborating in the EUROCARE II project, taking into account, whenever possible, the anatomical sub-site of origin of the tumours.

PATIENTS AND METHODS

Survival analysis was carried out on 35 004 head and neck (ICD 141, 143–148 and 161) cancer cases diagnosed between 1985 and 1989 in 17 countries as recorded by 44 population-based cancer registries. Some of these cover the whole country (Iceland, Finland, Denmark, Scotland, Slovenia, Slovakia, Estonia) or a large proportion of the country (England) whilst others cover up to 20% of the national population (those indicated with an asterisk in the relevant tables). Table 1 provides a breakdown of all head and neck cancer cases (35 782) by country and the major indicators of quality and completeness of information. The ratio of male to female patients was very high in Southern and Eastern countries, and low in Northern countries. Cases known on the basis of a death certificate only (DCO), as well as cases discovered at autopsy and cases first diagnosed with another tumour were not included. All cases were followed-up for at least 5 years.

Relative survival was computed as the ratio between the observed survival rate and the expected survival of the population of the same age, sex and country [13]. Overall (European) relative survival was estimated as the weighted average of the relative survival of the individual countries; weightings were proportional to the number of incident cases yearly diagnosed in each country. Age-standardised survival rates were calculated from age-specific rates for five age classes: 15-44, 45-54, 55–64, 65–74 and 75–99 years. The age distribution of cases in the entire European sample was used as the standard distribution for all periods, both sexes and all geographical areas. Cox proportional hazard models [14] were used to compare hazard rates between different countries or registries taking into account the different distribution of the anatomical site (and sub-site) of origin of the tumours.

Table 1. *Quality of data for head and neck cancer cases by country,* 1985–1989 *(EUROCARE* II*)*

Country	*n* of cases	% HV	% DCO	% Autopsy	% Lost to follow-up	Ratio M/F
Northern Europe						
Iceland	53	100	0.0	0.0	0.0	1.9
Finland	1312	99	0.2	0.5	0.0	2.7
Sweden*	620	100	0.0	1.0	0.0	3.3
Denmark	2881	99	0.0	0.0	0.0	2.8
U.K.						
Scotland	2714	93	1.6	0.0	0.0	1.9
England	9897	81	3.1	0.2	0.0	2.4
Western and Central Europe						
The Netherlands*	349	97	0.0	0.0	4.0	3.3
Germany*	971	98	1.2	0.2	0.0	6.0
Austria*	151	90	7.9	2.0	0.0	4.0
Switzerland*	566	99	0.1	0.9	3.2	4.6
France*	2595	98	–	0.0	8.0	12.0
Southern Europe						
Spain*	2608	96	3.0	0.2	0.3	12.9
Italy*	3830	91	1.6	0.0	0.5	6.1
Eastern Europe						
Slovenia	1647	97	1.5	0.2	0.7	10.5
Slovakia	4083	94	3.5	1.0	0.0	14.7
Poland*	727	92	1.8	0.0	1.2	5.1
Estonia	778	96	0.0	1.3	0.6	8.4
Europe†	35 782	–	–	–	–	–

Tongue (ICD 141), oral cavity (ICD 143-5), pharynx (ICD 145-8) and larynx (ICD 161) (cancers of the lip and major salivary glands are not included). HV, histologically verified; DCO, death certificate only. * < 20% of the national population covered. †Includes DCO and autopsy cases excluded from survival analysis. M/F, male/female.

Table 2. Incidence of head and neck cancers diagnosed in 1985–1989 *by country, anatomical site of origin and relevant ICD-IX fourth digit sub-site (%) (EUROCARE* II*)*

	Tongue			Mouth†		Oropharynx			Hypopharynx			Larynx		
Country	*n*	% Base (141.0)	% NOS (141.9)	*n*	% NOS (145.9)	*n*	% Tonsil (146.0)	% NOS (146.9)	*n*	% Pyriform sinus (148.1)	% NOS (148.9)	*n*	% Glottis (161.0)	% NOS (161.9)
Northern Europe														
Iceland	6	17	67	20	5	3	100	0	1	0	0	19	42	47
Finland	236	23	21	261	n.a.	74	92	7	93	n.a.	n.a.	754	n.a.	n.a.
Sweden*	89	21	63	157	41	53	66	32	59	5	95	222	65	23
Denmark	323	21	64	682	35	360	61	26	173	27	68	1225	49	17
U.K.														
Scotland	406	19	59	659	11	178	57	14	199	56	16	1132	38	41
England	1405	14	62	1855	12	735	68	16	882	53	13	4259	45	37
Western and Central Europe														
The Netherlands*	46	33	7	66	0	26	23	4	19	63	5	180	59	7
Germany*	180	39	38	218	11	116	70	21	93	18	78	316	30	42
Austria*	13	56	31	42	0	12	92	8	11	42	42	53	34	39
Switzerland*	102	30	16	98	7	93	48	24	74	53	39	182	46	14
France*	377	41	14	453	3	582	29	3	516	78	7	628	31	16
Southern Europe														
Spain*	298	25	26	386	11	236	46	27	200	66	24	1295	24	27
Italy*	399	29	30	492	29	344	54	13	199	53	33	2158	41	36
Eastern Europe														
Slovenia	211	40	15	311	2	364	19	5	204	58	9	485	35	11
Slovakia	603	38	3	678	1	610	54	2	437	46	16	1456	38	7
Poland*	88	10	89	60	5	101	40	52	16	18	82	425	3	92
Estonia	85	16	31	153	18	120	10	59	61	34	48	317	20	35

NOS, not otherwise specified. * < 20% of the national population covered. †ICD-IX 143–145.

RESULTS

Table 2 provides the number of cases by ICD 3-digit site and, as a further indicator of data quality, the proportion of cases with unspecified fourth digit sub-site. It also gives the proportion of cases coded to relevant sub-sites: base of tongue, tonsil, pyriform sinus and supraglottis. The proportion of unspecified sub-sites was fairly low for The Netherlands, France, Slovakia and Slovenia. U.K. data did not have sufficient detail for a proper analysis of cancer of the tongue but were fairly good for mouth and pharynx. Danish data were poorly detailed for tongue, mouth and pharynx but were sufficiently detailed for larynx. In Italy and Spain the data were fairly good for some registries, such as Varese, Mallorca and Basque Country but not for others. Some of the analyses, therefore, have been confined to cancer registries with less than 20% of unspecified sub-site cases.

The effect of gender on survival

The average European relative survival estimates for head and neck cancers by gender and anatomical site are given in Table 3. Patients with larynx cancer had the best 5-year survival (63–65% at 5 years) and hypopharynx cancer the worst (22–23%). Women had better 5-year survival than men, but not at 1 year.

Inter-country differences in survival

The age-adjusted 5-year relative survival of patients with cancer of the tongue, mouth and pharynx (ICD 141 + ICD 143–148) in men ranged from over 45% in Iceland, Sweden,

Table 3. One and 5-year age-standardised relative survival rates (%) for European patients with head and neck cancer: weighted average of cancer registries data from 17 countries, 1985–1989 (EUROCARE II)

	Relative survival			
	Men		Women	
	1-year (95% CI)	5-year (95% CI)	1-year (95% CI)	5-year (95% CI)
Tongue (ICD 141)	64 (61–67)	37 (33–42)	77 (73–81)	50 (45–59)
Oral cavity (ICD 143-5)	75 (71–78)	41 (37–45)	75 (71–79)	53 (48–58)
Oropharynx (ICD 146)	67 (64–69)	30 (27–34)	72 (66–79)	55 (38–53)
Hypopharynx (ICD 148)	63 (60–66)	22 (19–26)	61 (56–66)	23 (17–32)
Mouth or pharynx (ICD 141 & 143-148)	68 (67–70)	34 (32–36)	74 (71–76)	48 (44–51)
Larynx (ICD 161)	86 (85–87)	63 (61–65)	84 (80–87)	65 (61–70)

CI, confidence interval.

Table 4. Age-standardised 5-year relative survival for head and neck cancer patients in 17 European countries, 1985–1989. Age and sex standardised relative risks with and without adjustment for ICD 3-digit anatomical site (EUROCARE II)

	5-year relative survival				RR standardised for age and gender	
	Mouth and pharynx (ICD 141, 143–148)		Larynx (ICD 161)			
	Men	Women	Men	Women	Unadjusted for site (95% CI)	Adjusted for site (95% CI)
Northern Europe						
Iceland	45	50	74	–	0.73 (0.54–0.91)	0.72 (0.54–0.91)
Finland	35	54	60	54	1 (ref)	1 (ref)
Sweden*	50	63	74	65	0.86 (0.80–0.92)	0.82 (0.76–0.88)
Denmark	33	47	60	59	1.06 (1.02–1.11)	1.07 (1.03–1.10)
U.K.						
Scotland	35	44	64	59	1.05 (1.01–1.10)	1.06 (102–1.11)
England	37	46	66	64	0.94 (0.90–0.97)	0.94 (0.90–0.98)
Western and Central Europe						
The Netherlands*	47	46	76	100	0.68 (0.59–0.76)	0.72 (0.61–0.80)
Germany*	37	45	72	72	1.04 (0.99–1.10)	0.97 (0.91–1.02)
Austria*	47	52	58	–	0.84 (0.71–0.96)	0.80 (0.68–0.92)
Switzerland*	38	50	60	–	1.01 (0.94–1.07)	0.90 (0.84–0.97)
France*	32	57	51	58	1.29 (1.23–1.33)	1.04 (1.00–1.08)
Southern Europe						
Spain*	33	55	65	–	0.98 (0.93–1.02)	1.00 (0.96–1.05)
Italy*	35	46	67	65	0.83 (0.79–0.87)	0.89 (0.85–0.93)
Eastern Europe						
Slovenia	23	38	52	63	1.61 (1.56–1.66)	1.44 (1.40–1.49)
Slovakia	22	44	49	47	1.77 (1.73–1.80)	1.66 (1.62–1.70)
Poland*	20	30	44	59	1.34 (1.29–1.40)	1.50 (1.44–1.56)
Estonia	17	15	43	63	1.62 (1.56–1.67)	1.60 (1.55–1.66)

The Netherlands and Austria to less than 25% in Eastern countries (Table 4). Survival of male larynx cancer patients ranged from over 70% in Iceland, Sweden, The Netherlands and Germany to less than 50% in Slovakia, Poland and Estonia. For both sites the survival rates were lower in France (32 and 51%, respectively,) than in the U.K. (37 and 66%, respectively). France had the lowest rates in Western Europe, but such a high risk is likely to be mostly dependent on the different case mix of ICD 3-digit site. After adjustment for the relevant sites, there were no major differences between France and several other Western countries (Table 4). Such an adjustment for anatomical site confirmed that Sweden and the Netherlands had better survival, whilst Eastern countries had the worst.

Table 5. *Cox proportional regression analysis of survival of male patients with cancer of the oral cavity or pharynx diagnosed in* 1985–1989 *in eight European populations, with and without adjustment for ICD-IX fourth digit sub-site (EUROCARE* II*)*

	RR, unadjusted for sub-site (95% CI)	RR, adjusted for sub-site (95% CI)	*n* of subjects
Country			
Scotland	1.07 (1.01–1.12)	1.11 (1.06–1.17)	921
England, all areas	1 (ref)	1 (ref)	3112
The Netherlands, Eindhoven	0.82 (0.67–0.97)	0.80 (0.64–0.95)	109
France, Calvados and Doubs	1.10 (1.06–1.15)	0.99 (0.94–1.04)	989
Spain, Mallorca and Basque C	1.14 (1.07–1.20)	1.06 (0.99–1.12)	541
Italy, Varese	0.98 (0.90–1.07)	0.93 (0.85–1.02)	246
Slovakia	1.79 (1.75–1.83)	1.70 (1.66–1.74)	1648
Slovenia	1.61 (1.56–1.66)	1.39 (1.33–1.46)	849
Sub-sites			
Gum	(ICD-IX 143.0–143.9)	1 (ref)	618
Floor of mouth	(ICD-IX 144.0–144.9)	0.98 (0.91–1.04)	1766
Cheek and vestibule	(ICD-IX 145.0–145.1)	0.88 (0.78–0.97)	477
Hard palate and not specified	(ICD-IX 145.2 & 145.5)	0.75 (0.64–0.86)	321
Soft palate and uvula	(ICD-IX 145.3–145.4)	0.94 (0.85–1.03)	430
Retromolar area	(ICD-IX 145.6)	1.01 (0.91–1.11)	287
Mouth, overlapping	(ICD-IX 145.8)	1.38 (1.22–1.54)	71
Tonsil and pillar	(ICD-IX 146.0–146.2)	1.13 (1.06–1.20)	1578
Vallecula and junction	(ICD-IX 146.3–146.5)	1.27 (1.17–1.35)	292
Oropharynx, lateral and posterior	(ICD-IX 146.6–146.7)	1.72 (1.59–1.85)	106
Oropharynx, other parts	(ICD-IX 146.8)	1.47 (1.38–1.56)	405
Postcricoid region	(ICD-IX 148.0)	1.91 (1.80–2.02)	333
Pyriform sinus	(ICD-IX 148.1)	1.46 (1.39–1.53)	1381
Ariepiglottic fold	(ICD-IX 148.2)	1.25 (1.13–1.37)	139
Hypopharynx, posterior wall	(ICD-IX 148.3)	1.20 (1.06–1.35)	87
Hypopharynx	(ICD-IX 148.8)	2.01 (1.90–2.12)	160
Total			8451

RR, relative risk; CI, confidence interval.

Table 6. *Cox proportional regression analysis of survival of patients with cancer of the larynx diagnosed in* 1985–1989 *in nine European populations, with and without adjustment for ICD-IX fourth digit sub-site (EUROCARE* II*)*

		RR, unadjusted for sub-site (95% CI)	RR, adjusted for sub-site (95% CI)
Country			
Denmark		1 (ref)	1 (ref)
England, Mersey		0.75 (0.65–0.86)	0.80 (0.70–0.92)
The Netherlands, Eindhoven		0.55 (0.43–0.72)	0.58 (0.45–0.75)
Switzerland, Genova		0.75 (0.55–1.01)	0.73 (0.54–0.98)
France, Calvados and Doubs		1.11 (0.95–1.31)	0.97 (0.83–1.14)
Spain, Mallorca and Basque C		0.87 (0.76–1.00)	0.75 (0.65–0.86)
Italy, Varese		0.74 (0.62–0.88)	0.68 (0.57–0.80)
Slovakia		1.52 (1.36–1.68)	1.42 (1.28–1.59)
Slovenia		1.26 (1.10–1.45)	1.22 (1.04–1.42)
Sub-sites			
Glottis	(ICD-IX 161.0)		1 (ref)
Supraglottis	(ICD-IX 161.1)		2.21 (2.03–2.42)
Subglottis	(ICD-IX 161.2)		2.18 (1.71–2.78)
Laryngeal cartilage	(ICD-IX 161.3)		2.41 (1.08–5.40)
Overlapping areas	(ICD-IX 161.8)		2.06 (1.80–2.35)
Gender			
Women versus men		0.86 (0.77–0.99)	0.76 (0.67–0.87)

RR relative risk; CI, confidence interval.

The effect of sub-site on survival

Further analysis adjusting by sub-site was confined to the following countries and registries for which the proportion of unspecified cases was less than 20%: for mouth (excluding tongue), oro- and hypopharynx: U.K. registries, Eindhoven (The Netherlands), Calvados and Doubs (France), Mallorca and Basque Country (Spain) and Varese (Italy); for larynx: Denmark, Mersey (U.K.), Eindhoven, Calvados, Doubs, Mallorca, Basque Country and Varese. The results are shown in Tables 5 and 6. Table 5 shows that there were no major differences between Western countries (except The Netherlands) but survival was significantly lower in Eastern Europe. It confirmed the better prognosis for cancer of the palate and cheek mucosa with respect to gum and floor of mouth; the better prognosis of tonsil with respect to the other pharyngeal sites; and the dismal prognosis of hypopharynx, especially the retrocricoid area.

Table 6 shows that adjusting for glottis, supraglottis and other sub-sites, the relative hazard for Mediterranean countries was reduced with respect to registries in Northern and Central Europe.There was a significant interaction between some countries and gender. Analysing men and women separately (data not shown) showed that there was no difference between France and U.K. registries for men, whilst the RR for French women increased after adjusting for sub-site. For Eastern countries, the adjustment decreased the risk for men and increased it for women, because men had an higher proportion of supraglottic cancer and women a higher proportion of glottic cancer with respect to Northern and central Europe.

DISCUSSION

Survival of patients with head and neck cancers is difficult to study for several reasons. Firstly, the prognosis varies considerably according to the precise anatomical site of origin of the tumours, which affects the early appearance of symptoms and, therefore, the stage at diagnosis and the possibility of radical surgical resection. The distribution of such sites and sub-sites in European populations is far from uniform, so that geographical differences in survival may be largely due to a different case mix of specific sub-sites. Table 7 shows the range of incidence rates measured among male populations covered by cancer registries in Nordic countries, the U.K., Eastern countries and France, Italy and Spain [2]. The annual incidence rate of cancer of the oral mucosa (including tongue) ranges from approximately 2 in Finland and in several U.K. regions up to 12/100 000 men in some French registries. Cancers of the oropharynx and hypopharynx show even larger ranges, especially for pyriform sinus and oropharyngeal sites other than tonsil. Cancer of the larynx varies between 2.5 in Sweden and 18/100 000 men-year in Basque Country, but most of the variability depends on supraglottic cancer, whilst glottic cancer ranges only from approximately 2–5/100 000 [12]. Very few population data are available on the stage distribution of head and neck cancers by anatomical sub-site. The cancer registry of Norway has recently published the distribution by stage at diagnosis (localised disease, regional disease and distant spread) for squamous cell carcinoma diagnosed in 1953–1992, by several sub-sites: the proportion of distant spread was fairly low, ranging from 1% for glottic cancer and 2% for oral sites, to 4% for supraglottic, 5% for oropharynx and 6% for hypopharynx. The proportion of localised disease ranged from 85% for glottic to 26% for oropharynx and was 53% for supraglottic, 59% for tongue, 48% for floor of mouth, 58% for the other sites in the oral cavity and 35% for hypopharynx. The 5-year relative survival rates ranged accordingly from 77% for glottis cancer to 47% for supraglottic, 44% for oral cavity and tongue, 42% for the floor of mouth, 28% for oropharynx and 17% for hypopharynx [11]. These data are not directly comparable with the EUROCARE figures because of different age distribution and period of diagnosis, but show a very similar pattern of survival by anatomical site and sub-site. A recent clinical series of 640 oropharynx cancer cases confirmed a higher survival for the soft palate (54%), followed by the tonsillar region (42%) and base of tongue (33%) [10].

A second point is that head and neck mucosa is a region where the occurrence of multiple primaries is very frequent and such an event is a major determinant of prognosis and a major challenge for treatment [15, 16]. The occurrence of second primaries is likely to be due both to alcohol and tobacco and to inherited susceptibility, so that differential

Table 7. *Range of age-standardised incidence rates (per* 100 000 *World standard) of head and neck cancers in European males: highest and lowest registered rate for each cancer site and geographic area* [2]

Site (ICD-IX)		Tongue (141)	Oval cavity (143–145)	Oropharynx (146)	Hypopharynx (148)	Larynx (161)
Geographic area (no. of populations)						
Nordic countries (5 registries)	min	1.0 Finland	1.0 Finland	0.4 Finland	0.3 Iceland	2.5 Sweden
	max	1.5 Sweden	2.6 Denmark	1.7 Denmark	0.9 Norway	5.5 Denmark
U.K. (10 registries)	min	0.8 East Anglia	0.9 South West	0.5 East Anglia	0.4 Wessex	3.2 East Anglia
	max	2.0 W. Scotland	3.6 W. Scotland	1.1 Mersey	1.0 Mersey	6.9 W. Scotland
France (8 registries)	min	3.6 Tarn	2.8 Tarn	5.5 Herault	3.9 Herault	6.4 Tarn
	max	8.0 Bas-Rhin	12.4 Bas-Rhin	13.3 Somme	15.0 Calvados	14.8 Somme
Spain (9 registries)	min	2.1 Albacete	1.0 Albacete	1.0 Albacete	0.7 Albacete	11.6 Tarragona
	max	5.2 Asturias	4.9 Basque C	4.2 Asturias	4.3 Asturias	18.2 Basque C.
Italy (13 registries)	min	1.1 Ragusa	0.3 Macerata	0.1 Ragusa	0.1 Ragusa	4.8 Ragusa
	max	3.8 Veneto	8.4 Trieste	3.6 Varese	2.6 Parma	16.4 Veneto
Eastern countries (13 registries)	min	0.8 Poland Kielce	0.9 Poland Kielce	0.9 Poland Kielce	0.3 Poland Cracow	7.4 Czech Rep.
	max	5.1 Slovakia	5.4 Slovakia	6.7 Slovenia	4.4 Croatia	13.1 Croatia

prognosis may depend on both environmental and genetic factors. Besides the occurrence of other tumours in other areas of the upper aerodigestive tract, second primaries are frequently in the lung, especially for larynx cancer patients, and in the liver, which both have a very poor prognosis.

Thirdly, these tumours share three major risk factors, alcohol, tobacco [3] and low social class [17], which may have an independent effect on survival [5, 18]. Whether socio-economic deprivation *per se* or the risk factor behaviour associated with material deprivation is the cause of survival differences is not known. It seems clear, however, that comorbidity is a significant determinant of head and neck prognosis [19, 20]. The computation of relative survival dividing the observed survival by the corresponding survival of the general population may not be sufficient to correct for such competitive mortality. One should actually correct the observed survival using as a reference the survival of drinkers and smokers, which is not available. Moreover, alcohol and tobacco have different aetiological roles according to the sub-site: alcohol, for instance, is especially important for poor prognosis sub-sites, such as hypopharinx and epilarynx, as well as for the lower parts of oral and oropharyngeal mucosa, but is less important for glottic cancer [3].

Another problem with head and neck cancer is that misclassification of these cancer sites in current registries may be substantial; in Northern Italy, for instance, where these tumours are fairly frequent, the Lombardy (Varese Province) cancer registry has shown that in 28% of death certificates coded to larynx cancer, the underlying cause of death, following the ICD rules, should have been coded as cancer of other sites within the head and neck region [21]. However, part of the misclassification was due to the occurrence of multiple primaries in the head and neck region. A further 4% of deaths attributed to the larynx was due to tumours of distant sites, such as lung or oesophagus. Probably similar levels of misclassification are also present in several other registries.

Notwithstanding these various difficulties, some sound general conclusions can be drawn from the analysis of the EUROCARE II data. A major finding of this study was that survival of head and neck cancer patients diagnosed in Europe between 1985 and 1989 differed significantly between Eastern countries and the rest of Europe and the difference persisted after correcting for different sub-site distribution. This is consistent with data for most cancer sites [22] and is likely to be due to late diagnosis and to late referral or poor access of patients to adequately equipped treatment centres. Locally advanced head and neck cancer may be very difficult to treat and centralisation of treatment of such cases is likely to a be major determinant of survival. The EUROCARE data also suggest that in some Northern and Western countries, such as Sweden and The Netherlands, where centralisation of treatment has been realised since the 1980s, survival is better than elsewhere. There is no evidence that survival of men is worse in France and Spain than in U.K. populations, as it might appear from analyses that do not properly take into account the precise site of origin of the tumour [22]. At present we have little information on which to discuss whether the observed international survival differences are due to different extension of disease at diagnosis or to different access to effective treatment. The very low proportion of cases without specified sub-site in Eindhoven (The Netherlands) Calvados (France) and Varese (Italy) (6–9%) suggests that the proportion of very advanced local stage at diagnosis, for which the definition of the site of origin of the tumour would be impossible, was very low. As for Eastern countries, the low survival associated with a low proportion of unspecified sub-site, suggests that treatment facilities are not as effective as in the West. Such considerations would require detailed and internationally standardised information on the extent of disease, as well as on diagnostic staging procedures, that at present are not available.

A second important result of the present analysis is the detailed description of head and neck cancer prognosis by ICD 3-digit site and fourth digit sub-site in a fairly large series of cases (Tables 5 and 6). Within mouth and pharynx, better survival was seen for patients with cancer of the hard palate and cheek mucosa, followed by soft palate, floor of mouth and retromolar area, then by tonsil area, vallecula and junctional regions of oropharynx. The worst prognosis is for postcricoid region of hypopharynx, followed by pyriform sinus. For cancer of the ariepiglottic fold, survival was similar to that of the other epilaryngeal or junctional zones of the oropharynx.

Unfortunately sub-sites within tongue could not be directly compared because of the high frequency of unspecified sub-sites. However, confining the analysis to a few high quality cancer registries, showed that cancers arising on the tip or on the border of the tongue, as well as on the ventral surface, have a significantly higher survival (RR approximately 0.7) than those arising in other sub-sites. Finally, within larynx cancer, the relative risk of death was significantly higher for cancer of both supraglottis and subglottis, as well as for the rare laryngeal cartilage tumours, than for glottic cancer.

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APPENDIX

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