Trends of oral cavity, oropharyngeal and laryngeal cancer incidence in Scotland (1975 - 2012) - a socioeconomic perspective.

Mitana Purkayastha[1], Alex D. McMahon[1], John Gibson[1], David I. Conway[1]

Affiliations

[1] School of Medicine, Dentistry and Nursing, University of Glasgow, 378 Sauchiehall Street, Glasgow G2 3JZ, United Kingdom

Author Contact details:

M. Purkayastha

E-mail: m.purkayastha.1@research.gla.ac.uk

A D. McMahon

E-mail: Alex.McMahon@glasgow.ac.uk

J. Gibson

E-mail: John.Gibson.2@glasgow.ac.uk

D I. Conway

E-mail: David.Conway@glasgow.ac.uk

Corresponding Author

Mitana Purkayastha

Community Oral Health,

University of Glasgow Dental School,

Post-graduate Balcony, Level 9,

378 Sauchiehall Street,

Glasgow G2 3JZ,

United Kingdom.

Email: m.purkayastha.1@research.gla.ac.uk

Tel: ++44(0)141 211 9750

Abstract

Aim: To examine current incidence trends (1975–2012) of oral cavity (OCC), oropharyngeal (OPC) and laryngeal cancer in Scotland by socioeconomic status (SES).

Methods: We included all diagnosed cases of OCC (C00.3-C00.9, C02-C06 excluding C2.4), OPC (C01, C2.4, C09-C10, C14) and laryngeal cancer (C32) on the Scottish Cancer Registry (1975–2012) and annual mid-term population estimates by age, sex, geographic region and SES indices (Carstairs 1991 and Scottish Index of Multiple Deprivation 2009). Age-standardized incidence rates were computed and adjusted Poisson regression rate-ratios (RR) compared subsites by age, sex, region, SES and year of diagnosis.

Results: We found 28,217 individuals (19,755 males and 8462 females) diagnosed with head and neck cancer (HNC) over the study period. Between 1975 and 2012, relative to the least deprived areas, those living in the most deprived areas exhibited the highest RR (>double) of OCC, OPC and laryngeal cancer, and an almost dose-like response was observed between SES and HNC incidence. Between 2001 and 2012, this socioeconomic inequality tended to increase over time for OPC and laryngeal cancer but remained relatively unchanged for OCC. Incidence rates increased markedly for OPC, decreased for laryn-geal cancer and remained stable for OCC, particularly in the last decade. Males exhibited significantly higher RRs compared to females, and the peak age of incidence of OPC was slightly lower than the other subsites.

Conclusion: Contrary to reports that OPC exhibits an inverse socioeconomic profile, Scotland country-level data show that those from the most deprived areas consistently have the highest rates of head and neck cancers.

Keywords: Head and Neck Neoplasms, Incidence, Trends, Mouth Neoplasms, Oropharyngeal Neoplasms, Laryngeal Neoplasms

Introduction

Cancers of the oral cavity and oropharynx are amongst the most common cancers worldwide, with approximately 442,760 incident cases and 241,418 deaths reported in 2012 [1]. Collectively, these head and neck cancers are the seventh most common in terms of incidence and the ninth most common cause of death in the world [2].

Global incidence rates of oropharyngeal cancer (OPC) are rising, particularly in economically developed countries such as Canada, United States, Japan, Switzerland, Australia, England and parts of Eastern Europe [3-7]. Rates of oral cavity cancer (OCC) are also rising among men and women in some European countries, stabilising in certain Asian countries and decreasing in Canada and USA [4, 8].

Tobacco and alcohol consumption are the dominant risk factors for OCC [9], and are also a part of the aetiology for OPC along with human papillomavirus (HPV) infections [10]. Hashibe and Sturgis have suggested that this changing profile of head and neck cancer incidence can be explained by "controlling a tobacco epidemic while a human papillomavirus epidemic emerges" [11]. Moreover, the clinical perspective, recorded in a US case-series, is that the sociodemographic profile of head and neck cancer patients is also changing, with increasing numbers of patients, particularly with OPC diagnosis, having a younger, more socioeconomically affluent profile [12].

The most recent detailed analysis of incidence trends of oral cancer in Scotland examined rates between 1990 and 1999, and found that Scotland had the highest rates of oral cancer in the UK and also exhibited the greatest lifetime risk of developing oral cancer [13]. Overall, rates increased in both males and females between 1990 and 1999. However, this study combined both OCC and OPC into a single oral cancer definition in the trends analysis, reflecting the thinking at the time that these sites had a common aetiology.

The aim of this study was to examine the incidence burden and trends of OCC, OPC and laryngeal cancer in Scotland between 1975 and 2012 by key sociodemographic determinants available in the Scottish Cancer Registry: age, sex, area-based socioeconomic deprivation

indices, geographic region and year of diagnosis. Additionally, we aimed to compute future projected rates up to 2025 by the same determinants.

Methods

We collated data on all diagnosed cases of OPC, OCC and laryngeal cancer registered at the Scottish Cancer Registry between 1975 and 2012. Subsites were defined using three-digit ICD-10 codes and were anatomically classified into: oropharynx OPC (base of tongue C01, lingual tonsil C2.4, tonsil C09, oropharynx C10, pharynx C14); oral cavity OCC (inner lip C00.3-C00.9, other and unspecified parts of tongue C02, gum C03, floor of mouth C04, palate C05, other and unspecified parts of mouth C06); and larynx (C32). Additionally, all head and neck cancer (HNC) grouping included all of these subsites along with outer lip (C00.0-C00.2), salivary glands (C07, C08), nasopharynx (C11), piriform sinus (C12), hypopharynx (C13), and other and ill-defined sites of the lip, oral cavity and pharynx (C14). Age was grouped into five-year categories for the purpose of analysis. Based on NHS health board boundaries, the geographic regions were grouped into North (Grampian, Highland, Islands), East (Borders, Fife, Forth Valley, Lothian, Tayside), and West (Ayrshire and Arran, Dumfries & Galloway, Greater Glasgow & Clyde, Lanarkshire). Socioeconomic status was primarily measured using the area-based Carstairs Deprivation index grouped into deciles (14). This index is measured at the postcode sector level and takes four population census variables into account: male unemployment, households with no car, overcrowded households and the percentage of people in social classes IV and V. We also collated annual mid-year population estimates by age, sex, deprivation indices and geographic regions. Additional analysis was performed on cases diagnosed between 2000 and 2012 in order to utilize the more recently developed small area-based socioeconomic index, the Scottish Index of Multiple Deprivation (SIMD 2009) (15). This index is calculated taking seven domains of deprivation into consideration: income, employment, education, housing, health, crime and geographical access. It is measured at the data zone (neighbourhood) level (n=x of pop), which is a smaller population than the Carstairs postcode sector (n=x pop) (15).

Statistical Analysis

Age-standardized incidence rates and projected rates up to 2025 were calculated for all subsites by age, sex, deprivation, region, and year of diagnosis. Direct standardization was carried out using the European Standard population, to account for changes in the age composition of the population [16]. Adjusted Poisson regression rate-ratios were used to compare the subsites by age, sex, socioeconomic deprivation, geographical region and year of diagnosis. All statistical analyses were performed using SAS V9.3.

Results

Our study comprised of 28,217 individuals, of which 19,755 (70.2%) were males and 8,462 (29.9%) were females. The mean age was 63.8 years (standard deviation: ± 12.3 years). The age-standardised incidence rates of cancer per 100,000 individuals and the fully adjusted Poisson regression rate-ratios (RR) by sociodemographic characteristics are presented in Tables 1 and 2, respectively.

Peak incidence of OPC was observed in the 61-65 age-group, while that of OCC and laryngeal cancer were in the 71-75 age-group (Table 1). In the model, the 41-45 age-group was chosen as the reference category as the incidence rates in younger groups were very small, suggesting that this was a disease that primarily affected the older population. Regression analysis showed that the rates of OPC were more than double in the 61-65 age-group (RR 2.34, 95% CI 2.08-2.63) compared to the reference category (41-45 age-group), and this was statistically significant (Table 2). The highest rate-ratios for OCC (RR 3.54, 95% CI 3.20-3.91) and laryngeal cancer (RR 4.74, 95% CI 4.30-5.23) were observed in the 76-80 and 71-75 age-groups, respectively, relative to the reference group (Table 2).

Males were found to exhibit higher incidence rates than females in all subsites (Table 1). The rates in males were more than three times that of females (RR 3.10, 95% CI 2.90-3.30) for OPC, more than double for OCC (RR 2.11, 95% CI 2.02-2.20), and 4.77 times for laryngeal cancer (RR 4.77, 95% CI 4.54-5.01) (Table 2).

No major differences in incidence burden were observed between the different geographic regions, with rate-ratios of the North, East and West health board regions being similar irrespective of subsite.

The rate-ratios of OPC (RR 2.49, 95%CI 2.18-2.86) and OCC (RR 2.40, 95%CI 2.18-2.65) in the most deprived (Carstairs 1) areas were significantly higher than those in the least deprived (Carstairs 10) areas across all subsites. Moreover, a dose-like effect was observed, with rates of cancer increasing with increasing deprivation (Table 2). This socioeconomic inequality persisted in the analysis of cases diagnosed between 2001 and 2012 using SIMD. Moreover, the socioeconomic gap widened in OPC (RR 3.33, 95% CI 2.72-4.07) and laryngeal cancer (RR 4.98; 95% CI 4.15-5.97), but remained relatively unchanged for OCC (RR 2.69; 95% CI 2.31-3.13) over the past decade (Figure 2).

Incidence rates of OPC increased by 245% between 1975 and 2012 (RR 3.45, 95% CI 2.66-4.48), while rates of OCC showed a smaller increase of 86% over the same period (RR 1.86, 95% CI 1.53-2.26). Both of these increases were statistically significant (Figure 1). Rates of laryngeal cancer increased by only 12%, but this was not statistically significant (RR 1.12, 95% CI 0.92-1.35). Between 2001 and 2012, incidence rates of OPC increased by 85% (RR 1.85, 95% CI 1.53-2.25), rates of OCC remained relatively stable (RR 1.10, 95% CI 0.94-1.28), and rates of laryngeal cancer decreased by 23% (RR 0.77, 95% CI 0.65-0.90).

Incidence projections up to 2025 show an expected continuation with increases in the rates of HNC, and this appears to be largely driven by a rapid increase in the rates of OPC. Moreover, OPC is expected to overtake the rates of OCC, which continue to remain relatively stable. Rates of laryngeal cancer were expected to decrease over the projection period (Figure 3).

Discussion

By 2012, the incidence rates of OPC had overtaken those of laryngeal cancer and were nearly on par with OCC incidence. Moreover, by 2025 the projected incidence rates of OPC are expected to continue to rise rapidly and bypass rates of OCC which are expected to continue to remain relatively stable. Rates of laryngeal cancer are expected to decrease over the same time

period. The peak age of incidence of OPC was slightly younger (5-10 years) than for the other subsites, and rates were consistently higher in males compared to females irrespective of subsite.

Our study was the first national descriptive epidemiology study to examine trends in HNC by SES. We observed socioeconomic inequality in incidence across all subsites, with the most deprived areas consistently exhibiting the highest rates of head and neck cancer relative to the least deprived areas.

An age-period-cohort analysis of global data reported similar overall trends of increasing OPC and stabilising OCC [4]. In England, a detailed cancer registry analysis reported that the incidence rates of head and neck cancer (HNC) increased by 58.9% in the sixteen year study period, with the greatest increase in rates of OPC (average annual percentage change = +7.3% in males and +6.5% in females) [3]. Our results showed an increase of 32.13% in HNC rates in Scotland over the same time period (1995 to 2011), and this was largely driven by a rapid increase in the rates of OPC. HNC rates were also expected to continue to rise up to 2025 in England, with the largest increase being observed in rates of OPC, while OCC was predicted to stabilize in men and continue to increase in women. Moreover, rates of OPC were seen to be higher in younger individuals (< 60 years) in England [3]. Our projection estimates showed a similar increase in rates of HNC, driven largely by a rapid rise in rates of OPC, in Scotland. Moreover, the peak incidence of OPC in Scotland was observed in the 61-65 age-group, and this was also in agreement with previous studies. It has been suggested that this plateauing in rates of OCC may be a result of the decreasing global rates of smoking observed in the recent past, and the increase in rates of OPC possibly reflect the changes in sexual behaviours among recent birth cohorts, which in turn increases risk of exposure to oral HPV infection [3, 4].

We also observed higher rates amongst men, which was in agreement with another retrospective analysis conducted by Gillison et al in USA [17]. This difference in incidence rates could be explained in part by the greater prevalence of HPV among men compared to women [5, 11, 18].

However, in contrast to a previous small clinical series [12], we found that socioeconomic inequalities in rates of cancer persisted irrespective of cancer subsite in Scotland, with the most

deprived areas of the country consistently showing the highest rate-ratios relative to the least deprived areas. Although previous studies have examined the trends of HNC and subsites in Scotland, they have combined OCC and OPC, which may have masked the differential rates by subsite [13].

Geographic area-based deprivation indices result in all individuals living within a certain area being assigned the same score. Interpretation of these area-based measures is complex. When used as a surrogate individual measure, it may be inferred that all persons living in a certain socioeconomic area have the same individual socioeconomic status, and this has been described as an 'ecological fallacy' [19, 20]. However, the ecological interpretation can have some advantages in terms of indicating the social and physical environment or circumstances, for example, adequate access to health care services. Ideally, a combination of individual and area-based socioeconomic measures would be combined in a multi-level analysis to take account of individual and area effects.

The strengths of this study are based on the high quality national data which provides a population representative cohort over several decades. The quality indicators for registration of head and neck cancer tumours at the Scottish Cancer Registry are high, with approximately 85% of cases being microscopically confirmed and less than 2% Death Certificate Only registrations [21, 22]. Moreover, several studies have provided evidence of the high, and constantly improving, case-ascertainment [23-25]. The limitations of this study include the lack of data on tumour HPV positivity, behavioural factors (e.g. tobacco and alcohol consumption), and individual measures of socioeconomic status [26]. Data on HPV and behaviours would have allowed estimation of the proportion of changes in incidence rates that could be attributed to various risk factors and socioeconomic determinants. This information may help provide a clearer picture of what is driving the changing trends of head and neck cancer.

Conclusion

In conclusion, this study shows the changing trends in the burden and determinants of HNC. OPC is an emerging public health problem, with rates dramatically increasing in Scotland.

Despite previous reports, the sociodemographic determinants of oropharyngeal cancer are not substantially different from other HNCs, particularly in relation to gender and SES profile

Acknowledgements

The authors would like to thank the Scottish Cancer Registry for data access and NHS Education for Scotland for funding this study.

Figure 1: European age-standardised incidence rates (EASR) for each subsite over time from 1975 to 2012. (HNC: All head & neck cancer, OPC: Oropharyngeal cancer, OCC: Oral cavity cancer

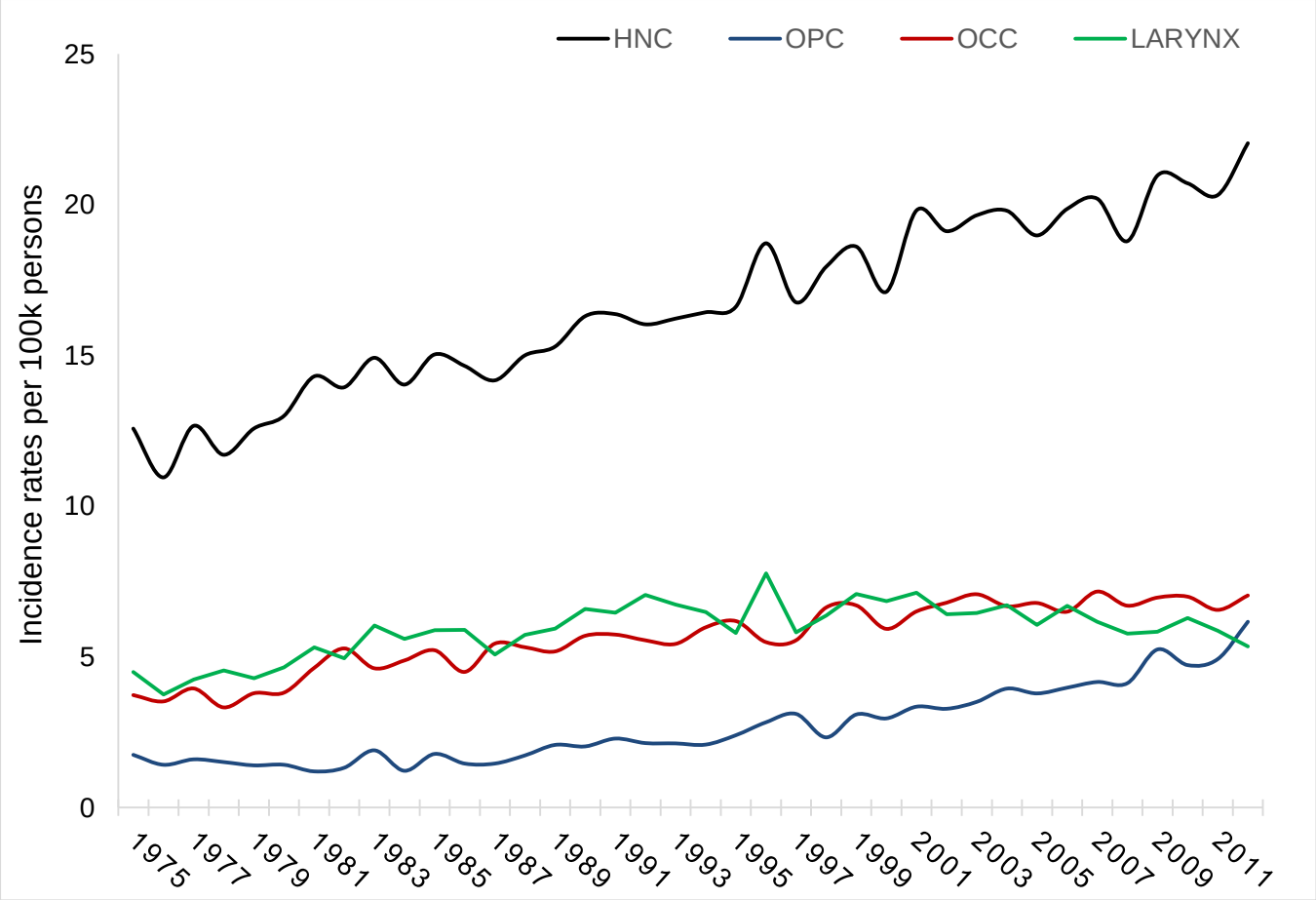

Figure 2: Incidence rates for each subsite by Scottish Index of Multiple Deprivation (SIMD) 2009, where 1= most deprived and 10=least deprived (2001-2012). (HNC: All head & neck cancer, OPC: Oropharyngeal cancer, OCC: Oral cavity cancer)

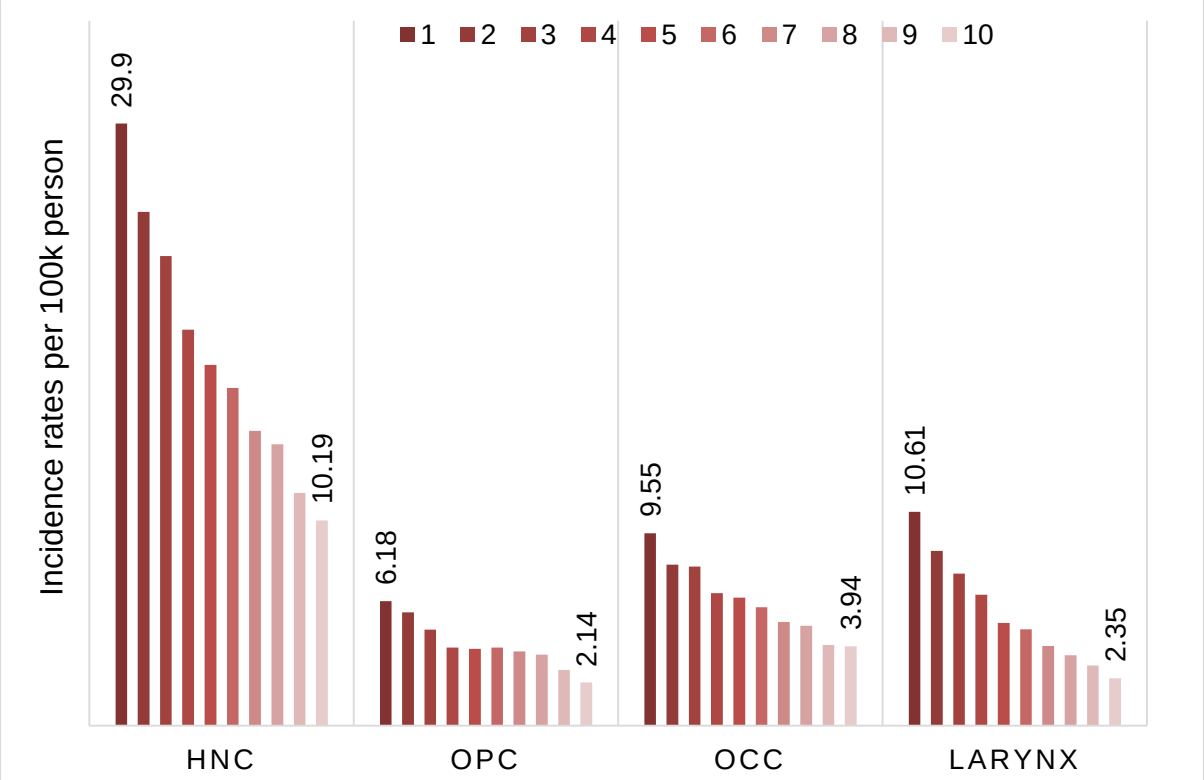

Figure 3: Incidence rates per 100k persons between 2001-2012 (bold lines) and projected rates (dotted lines) up to 2025 for each subsite (HNC: All head & neck cancer, OPC : Oropharyngeal cancer, OCC: Oral cavity cancer)

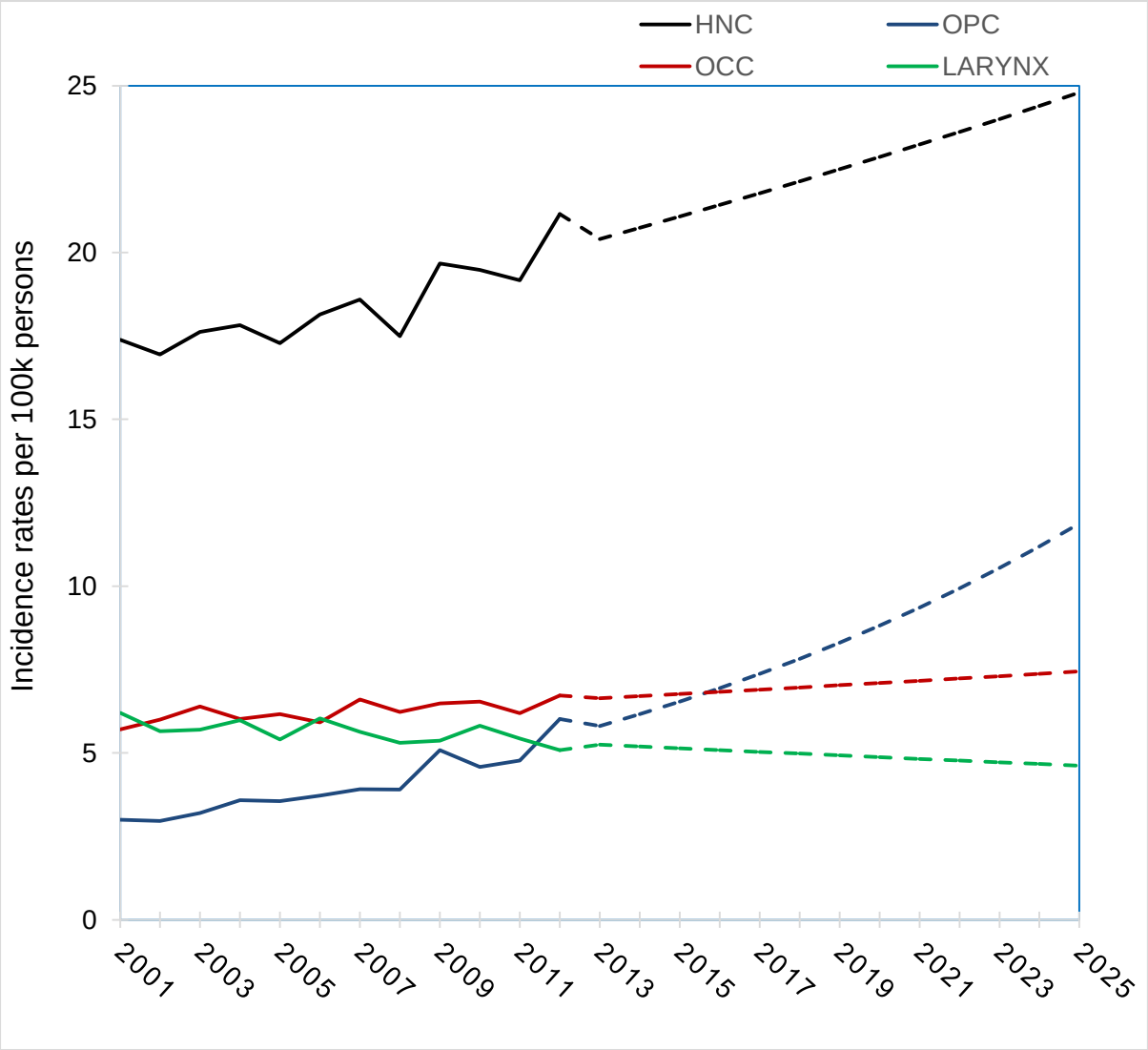

Table 1: EASR per 100,000 person-years by age, sex, geographic region, deprivation (Carstairs 1991), and year of diagnosis (1975-2012)

	HNC		OPC		OCC		Larynx	
	N	**Rate**	**N**	**Rate**	**N**	**Rate**	**N**	**Rate**
Age								
0-25	135	0.28	7	0.01	35	0.07	5	0.01
26-30	87	0.94	2	0.02	29	0.31	5	0.05
31-35	145	1.54	9	0.10	44	0.47	16	0.17
36-40	294	3.46	36	0.42	79	0.93	67	0.79
41-45	537	6.39	80	0.96	177	2.11	150	1.79
46-50	1185	15.13	179	2.32	408	5.27	402	5.19
51-55	1817	22.80	261	3.38	603	7.79	674	8.67
56-60	2484	32.17	349	4.72	756	10.19	1001	13.41
61-65	2648	38.64	348	5.37	803	12.29	1091	16.62
66-70	2736	41.80	328	5.26	866	13.84	1119	17.75
71-75	2334	45.52	260	5.27	747	15.11	935	18.79
76-80	1656	44.71	175	4.81	609	16.66	572	15.65
81-85+	1015	30.61	109	3.30	421	12.75	293	8.88
Sex								
Male	19755	20.67	3352	3.60	5851	6.28	7744	8.29
Female	8462	8.41	1272	1.27	3467	3.46	2009	2.01
Region								
North	9768	13.55	1547	2.18	3201	4.50	3375	4.74
East	4431	14.56	786	2.59	1467	4.84	1286	4.24
West	14018	14.95	2291	2.50	4650	5.06	5092	5.53
Carstairs								
1	4254	21.53	682	3.51	1354	6.95	1644	8.42
2	3499	17.40	534	2.77	1122	5.80	1337	6.89
3	3059	15.44	490	2.53	983	5.07	1107	5.69
4	3050	15.56	545	2.83	948	4.92	1090	5.65
5	2676	13.63	431	2.23	893	4.61	901	4.64
6	2717	14.00	426	2.22	939	4.90	927	4.83
7	2483	12.68	426	2.20	855	4.41	766	3.95
8	2453	12.62	402	2.09	848	4.41	785	4.08
9	2154	11.06	364	1.88	736	3.81	656	3.39
10	1872	9.63	324	1.68	640	3.31	540	2.79

Year								
1975	502	12.57	69	1.75	140	3.73	180	4.50
1976	439	10.95	55	1.42	135	3.52	153	3.75
1977	521	12.66	63	1.60	155	3.95	173	4.25
1978	485	11.70	60	1.51	130	3.32	187	4.55
1979	513	12.57	55	1.40	148	3.79	176	4.29
1980	531	12.99	55	1.42	152	3.81	190	4.65
1981	594	14.30	49	1.20	184	4.63	220	5.32
1982	585	13.94	54	1.32	215	5.28	203	4.95
1983	634	14.92	77	1.90	188	4.62	249	6.04
1984	589	14.03	51	1.22	200	4.88	231	5.60
1985	643	15.03	74	1.78	215	5.22	4.87	5.89
1986	621	14.65	61	1.46	187	4.50	246	5.90
1987	608	14.17	62	1.46	226	5.44	214	5.08
1988	651	15.00	73	1.73	224	5.32	242	5.73
1989	674	15.29	88	2.08	219	5.18	252	5.94
1990	718	16.30	86	2.03	242	5.70	278	6.59
1991	720	16.37	97	2.29	244	5.74	274	6.47
1992	710	16.03	92	2.14	236	5.55	302	7.06
1993	719	16.22	91	2.13	234	5.43	288	6.73
1994	739	16.43	91	2.09	259	5.98	282	6.49
1995	750	16.61	104	2.40	267	6.19	253	5.79
1996	864	18.72	124	2.83	271	5.49	340	7.77
1997	768	16.76	138	3.11	245	5.55	255	5.81
1998	826	17.94	103	2.33	296	6.64	279	6.37
1999	865	18.61	138	3.09	298	6.71	313	7.09
2000	804	17.11	133	2.96	267	5.93	305	6.85
2001	880	19.81	152	3.35	289	6.51	314	7.13
2002	858	19.12	150	3.28	304	6.80	286	6.41
2003	893	19.65	162	3.51	324	7.08	289	6.46
2004	906	19.80	182	3.95	306	6.68	304	6.71
2005	883	18.98	182	3.79	315	6.79	276	6.06
2006	931	19.86	191	3.98	304	6.50	310	6.69
2007	961	20.20	202	4.17	341	7.17	291	6.17
2008	910	18.79	203	4.13	324	6.70	276	5.77
2009	1029	20.97	266	5.25	339	6.97	281	5.83
2010	1025	20.71	241	4.73	344	7.00	306	6.29
2011	1016	20.32	253	4.93	328	6.56	288	5.86
2012	1124	22.04	320	6.17	357	7.04	270	5.35

EASR: European age standardized rates, HNC: Head & neck cancer; OPC: cancer; OCC: Oral cavity cancer; N: Number of events

Table 2: Adjusted Poisson regression rate-ratios for subsites by age, sex, geographic region, deprivation (Carstairs 1991), and year of diagnosis (1975-2012)

	HNC			OPC			OCC			LARYNX		
	RR	**95% CI**	***p***	**RR**	**95% CI**	***p***	**RR**	**95% CI**	***p***	**RR**	**95% CI**	***p***
Age												
0-25	0.02	0.02-	**<.001**	0.01	0.00-0.01	**<.00**	0.02	0.01-	**<.001**	0.00	0.00-	**<.001**
26-30	0.07	0.05-	**<.001**	0.02	0.01-0.03	**<.00**	0.07	0.05-	**<.001**	0.02	0.01-	**<.001**
31-35	0.10	0.09-	**<.001**	0.04	0.03-0.07	**<.00**	0.10	0.08-	**<.001**	0.04	0.02-	**<.001**
36-40	0.24	0.21-	**<.001**	0.17	0.13-0.22	**<.00**	0.20	0.17-	**<.001**	0.17	0.13-	**<.001**
41-45	0.46	0.43-	**<.001**	0.45	0.38-0.53	**<.00**	0.45	0.39-	**<.001**	0.37	0.32-	**<.001**
46-50	-			-			-			-		
51-55	1.62	1.53-	**<.001**	1.62	1.44-1.83	**<.00**	1.58	1.43-	**<.001**	1.82	1.64-	**<.001**
56-60	2.38	2.25-	**<.001**	2.21	1.97-2.49	**<.00**	2.31	2.10-	**<.001**	3.02	2.74-	**<.001**
61-65	2.79	2.65-	**<.001**	2.34	2.08-2.63	**<.00**	2.73	2.49-	**<.001**	3.73	3.39-	**<.001**
66-70	3.06	2.90-	**<.001**	2.19	1.93-2.47	**<.00**	3.04	2.77-	**<.001**	4.29	3.90-	**<.001**
71-75	3.39	3.21-	**<.001**	2.03	1.78-2.32	**<.00**	3.30	3.00-	**<.001**	4.74	4.30-	**<.001**
76-80	3.44	3.24-	**<.001**	1.97	1.71-2.28	**<.00**	3.54	3.20-	**<.001**	4.32	3.89-	**<.001**
81-85+	2.36	2.20-	**<.001**	1.08	0.90-1.29	0.39	2.66	2.39-	**<.001**	2.56	2.26-	**<.001**
Sex												
Male	2.72	2.66-	**<.001**	3.10	2.90-3.30	**<.00**	2.11	2.02-	**<.001**	4.77	4.54-	**<.001**
Female (ref.)	-			-			-			-		
Region												
North	-			-			-			-		
East	0.85	0.82-	**<.001**	0.81	0.74-0.88	**<.00**	0.88	0.83-	**<.001**	1.01	0.95-	0.738
West	0.81	0.78-	**<.001**	0.85	0.78-0.92	**<.00**	0.89	0.84-	**<.001**	0.98	0.92-	0.527
Carstairs 1991												
1	2.59	2.45-	**<.001**	2.49	2.18-2.86	**<.00**	2.40	2.18-	**<.001**	3.34	3.02-	**<.001**
2	1.83	1.72-	**<.001**	1.83	1.59-2.11	**<.00**	1.86	1.69-	**<.001**	2.50	2.26-	**<.001**
3	1.66	1.57-	**<.001**	1.67	1.45-1.92	**<.00**	1.62	1.47-	**<.001**	2.07	1.87-	**<.001**
4	1.66	1.57-	**<.001**	1.85	1.61-2.12	**<.00**	1.56	1.41-	**<.001**	2.06	1.86-	**<.001**
5	1.47	1.38-	**<.001**	1.44	1.25-1.66	**<.00**	1.47	1.32-	**<.001**	1.71	1.54-	**<.001**
6	1.42	1.34-	**<.001**	1.35	1.17-1.56	**<.00**	1.47	1.33-	**<.001**	1.70	1.53-	**<.001**
7	1.30	1.22-	**<.001**	1.32	1.15-1.53	**<.00**	1.33	1.20-	**<.001**	1.39	1.24-	**<.001**
8	1.26	1.19-	**<.001**	1.24	1.07-1.43	**0.00**	1.30	1.17-	**<.001**	1.40	1.26-	**<.001**
9	1.12	1.05-	**<.001**	1.13	0.97-1.31	0.10	1.14	1.02-	**0.019**	1.19	1.06-	**0.003**
10 (ref.)	-			-			-			-		

Year												
1975 (ref.)	-			-			-			-		
1976	0.88	0.77-	**0.049**	0.79	0.56-1.13	0.20	0.96	0.76-	0.732	0.84	0.68-	0.118
1977	1.02	0.91-	0.698	0.90	0.64-1.27	0.56	1.10	0.87-	0.426	0.95	0.77-	0.645
1978	0.94	0.83-	0.355	0.86	0.61-1.22	0.40	0.92	0.72-	0.475	1.00	0.82-	0.972
1979	1.01	0.89-	0.872	0.79	0.55-1.12	0.19	1.04	0.83-	0.736	0.96	0.78-	0.699
1980	1.04	0.92-	0.507	0.79	0.55-1.12	0.18	1.06	0.84-	0.606	1.04	0.84-	0.736
1981	1.15	1.02-	**0.024**	0.70	0.48-1.00	0.05	1.28	1.03-	**0.027**	1.19	0.97-	0.091
1982	1.11	0.99-	0.080	0.77	0.54-1.09	0.14	1.49	1.20-	**<.001**	1.09	0.89-	0.427
1983	1.18	1.05-	**0.006**	1.09	0.79-1.51	0.60	1.30	1.04-	**0.020**	1.31	1.08-	0.006
1984	1.13	1.00-	**0.052**	0.72	0.50-1.03	0.07	1.37	1.10-	**0.005**	1.24	1.02-	**0.035**
1985	1.19	1.06-	**0.003**	1.04	0.75-1.44	0.82	1.45	1.18-	**<.001**	1.29	1.06-	**0.010**
1986	1.17	1.04-	0.007	0.85	0.60-1.20	0.36	1.27	1.02-	**0.034**	1.29	1.06-	**0.010**
1987	1.14	1.01-	**0.034**	0.86	0.61-1.21	0.38	1.52	1.23-	**<.001**	1.11	0.91-	**0.293**
1988	1.20	1.07-	**0.002**	1.01	0.73-1.40	0.95	1.50	1.21-	**<.001**	1.25	1.03-	**0.024**
1989	1.22	1.08-	**<.001**	1.21	0.88-1.66	0.23	1.45	1.17-	**<.001**	1.29	1.07-	**0.009**
1990	1.28	1.14-	**<.001**	1.18	0.86-1.62	0.30	1.60	1.30-	**<.001**	1.42	1.18-	**<.001**
1991	1.29	1.15-	**<.001**	1.33	0.97-1.81	0.07	1.61	1.30-	**<.001**	1.40	1.16-	**<.001**
1992	1.26	1.12-	**<.001**	1.25	0.92-1.71	0.16	1.55	1.25-	**<.001**	1.51	1.25-	**<.001**
1993	1.26	1.13-	**<.001**	1.23	0.90-1.68	0.19	1.52	1.23-	**<.001**	1.44	1.19-	**<.001**
1994	1.29	1.16-	**<.001**	1.22	0.89-1.67	0.21	1.67	1.36-	**<.001**	1.39	1.15-	**<.001**
1995	1.29	1.16-	**<.001**	1.38	1.02-1.88	**0.03**	1.72	1.40-	**<.001**	1.23	1.01-	**0.037**
1996	1.46	1.30-	**<.001**	1.63	1.22-2.19	**0.00**	1.71	1.40-	**<.001**	1.65	1.37-	**<.001**
1997	1.32	1.18-	**<.001**	1.80	1.35-2.41	**<.00**	1.55	1.26-	**<.001**	1.25	1.03-	**0.026**
1998	1.39	1.25-	**<.001**	1.34	0.99-1.82	**0.05**	1.85	1.51-	**<.001**	1.35	1.11-	**0.002**
1999	1.44	1.29-	**<.001**	1.77	1.33-2.37	**<.00**	1.86	1.52-	**<.001**	1.51	1.25-	**<.001**
2000	1.32	1.18-	**<.001**	1.70	1.27-2.27	**<.00**	1.65	1.34-	**<.001**	1.44	1.19-	**<.001**

RR: Rate-ratio; *p:* p value; HNC: Head & neck cancer; OPC: Oropharyngeal cancer; OCC: Oral cavity cancer.
Bold values represent statistical significance.

Table 3: Subgroup analysis- Adjusted Poisson regression rate-ratios for subsites by age, sex, geographic region, deprivation (SIMD 2009), and year of diagnosis (2001-2012)

	HNC			OPC			OCC			LARYX		
	RR	**95% CI**	***p***	**RR**	**95% CI**	***p***	**RR**	**95% CI**	***p***	**RR**	**95 % CI**	***p***
Age												
0-25	0.02	0.02-0.03	**<0.001**	0	0.00-0.01	**<0.001**	0.02	0.01-0.03	**<0.001**	0	0.00-0.01	**<0.001**
26-30	0.07	0.05-0.10	**<0.001**	0.02	0.01-0.06	**<0.001**	0.09	0.06-0.14	**<0.001**	0.04	0.01-0.09	**<0.001**
31-35	0.1	0.08-0.13	**<0.001**	0.05	0.02-0.08	**<0.001**	0.13	0.09-0.19	**<0.001**	0.05	0.02-0.10	**<0.001**
36-40	0.24	0.20-0.28	**<0.001**	0.16	0.11-0.22	**<0.001**	0.25	0.19-0.33	**<0.001**	0.2	0.14-0.30	**<0.001**
41-45	0.51	0.45-0.58	**<0.001**	0.47	0.37-0.58	**<0.001**	0.52	0.42-0.65	**<0.001**	0.44	0.33-0.59	**<0.001**
46-50 (ref)	-			-			-					
51-55	2	1.83-2.20	**<0.001**	1.81	1.55-2.12	**<0.001**	1.82	1.55-2.14	**<0.001**	2.34	1.93-2.84	**<0.001**
56-60	2.94	2.69-3.21	**<0.001**	2.23	1.91-2.61	**<0.001**	2.83	2.43-3.30	**<0.001**	4.08	3.40-4.89	**<0.001**
61-65	3.6	3.30-3.92	**<0.001**	2.37	2.03-2.77	**<0.001**	3.51	3.02-4.07	**<0.001**	5.31	4.44-6.34	**<0.001**
66-70	3.71	3.40-4.06	**<0.001**	2.01	1.70-2.38	**<0.001**	3.65	3.14-4.25	**<0.001**	6.35	5.31-7.59	**<0.001**
71-75	3.81	3.48-4.18	**<0.001**	1.65	1.37-1.98	**<0.001**	3.7	3.17-4.33	**<0.001**	6.69	5.58-8.01	**<0.001**
76-80	3.59	3.26-3.96	**<0.001**	1.66	1.36-2.03	**<0.001**	3.6	3.06-4.25	**<0.001**	6.17	5.10-7.46	**<0.001**
81-85+	3.35	3.00-3.73	**<0.001**	1	0.76-1.33	0.977	3.92	3.28-4.68	**<0.001**	4.73	3.80-5.89	**<0.001**
Sex												
Male	2.81	2.70-2.92	**<0.001**	3.31	3.02-3.62	**<0.001**	1.82	1.71-	**<0.001**	4.6	4.24-5.00	**<0.001**
Female(ref	-											
Region												
North (ref.)	-			-			-			-		
East	1.06	1.00-1.12	**0.05**	0.86	0.77-0.97	**0.012**	1.1	1.00-1.21	**0.057**	1.2	1.08-1.33	**<0.001**
West	1.07	1.02-1.14	**0.011**	0.93	0.83-1.04	0.185	1.11	1.01-1.22	**0.028**	1.21	1.09-1.34	**<0.001**
SIMD												
1	3.3	3.01-3.62	**<0.001**	3.33	2.72-4.07	**<0.001**	2.69	2.31-3.13	**<0.001**	4.98	4.15-5.97	**<0.001**
2	2.6	2.37-2.85	**<0.001**	2.83	2.31-3.46	**<0.001**	2.08	1.78-2.43	**<0.001**	3.75	3.11-4.51	**<0.001**
3	2.31	2.10-2.54	**<0.001**	2.33	1.89-2.86	**<0.001**	2	1.71-2.33	**<0.001**	3.19	2.64-3.84	**<0.001**
4	1.89	1.72-2.08	**<0.001**	1.82	1.47-2.25	**<0.001**	1.62	1.38-1.90	**<0.001**	2.67	2.21-3.23	**<0.001**
5	1.73	1.57-1.91	**<0.001**	1.74	1.41-2.16	**<0.001**	1.58	1.35-1.86	**<0.001**	2.13	1.75-2.60	**<0.001**
6	1.58	1.43-1.75	**<0.001**	1.72	1.39-2.13	**<0.001**	1.44	1.22-1.69	**<0.001**	1.96	1.60-2.39	**<0.001**
7	1.36	1.23-1.51	**<0.001**	1.61	1.30-2.00	**<0.001**	1.25	1.05-1.47	**0.01**	1.6	1.30-1.96	**<0.001**
8	1.35	1.22-1.49	**<0.001**	1.6	1.29-1.99	**<0.001**	1.24	1.04-1.46	**0.014**	1.47	1.19-1.81	**<0.001**
9	1.12	1.00-1.25	**0.042**	1.25	1.00-1.57	**0.053**	1.01	0.84-1.21	0.923	1.26	1.01-1.56	**0.041**
10 (ref.)	-			-			-			-		

Year												
2001 (ref.)	-			-			-			-		
2002	0.97	0.88-1.07	0.52	0.98	0.78-1.23	0.864	1.05	0.89-1.23	0.586	0.91	0.77-1.07	0.235
2003	1	0.91-1.10	0.977	1.05	0.84-1.31	0.667	1.11	0.94-1.30	0.216	0.91	0.78-1.07	0.252
2004	1.01	0.92-1.10	0.906	1.17	0.94-1.45	0.163	1.03	0.88-1.21	0.689	0.95	0.81-1.11	0.516
2005	0.97	0.88-1.06	0.516	1.15	0.93-1.43	0.198	1.05	0.90-1.23	0.53	0.85	0.73-1.00	**0.054**
2006	1.01	0.92-1.11	0.798	1.2	0.97-1.48	0.101	1.01	0.86-1.18	0.944	0.95	0.81-1.11	0.516
2007	1.03	0.91-1.13	0.478	1.25	1.01-1.54	**0.039**	1.12	0.95-1.31	0.169	0.88	0.75-1.04	0.126
2008	0.97	0.88-1.06	0.464	1.24	1.00-1.53	**0.046**	1.05	0.89-1.23	0.571	0.83	0.70-0.97	**0.021**
2009	1.08	0.99-1.18	0.101	1.6	1.31-1.95	**<0.001**	1.08	0.92-1.27	0.326	0.83	0.71-0.98	**0.024**
2010	1.06	0.97-1.16	0.209	1.43	1.17-1.75	**<0.001**	1.08	0.93-1.27	0.317	0.89	0.76-1.04	0.155
2011	1.04	0.95-1.13	0.442	1.48	1.21-1.81	**<0.001**	1.02	0.87-1.19	0.814	0.83	0.71-0.97	**0.021**
2012	1.13	1.04-1.24	**0.005**	1.85	1.53-2.25	**<0.001**	1.1	0.94-1.28	0.242	0.77	0.65-0.90	**0.001**

SIMD: Scottish index of multiple deprivation; RR: Rate-ratio; *p:* p value; HNC: Head & neck cancer; OPC: Oropharyngeal cancer; OCC: Oral cavity cancer. Bold values represent statistical significance.

Conflict of Interest Statement

The authors declare no conflicts of interest.

References

[1] Ferlay J, Soerjomataram I, Ervik M, *et al;* International Agency for Research on Cancer GLOBOCAN 2012 v1.0. Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 http://globocan.iarc.fr/Default.aspx; 2013 [Accessed: 5th April 2016]

[2] Stewart, B. and Wild, C.P. (eds.), International Agency for Research on Cancer, WHO. (2014) *World Cancer Report 2014* [Online]. http://www.thehealthwell.info/node/725845 [Accessed: 5th April 2016].

[3] Louie KS, Mehanna H, Sasieni P. Trends in head and neck cancers in England from 1995 to 2011 and projections up to 2025. *Oral Oncol* 2015; 51(4): 341-348.

[4] Chaturvedi AK, Anderson WF, Lortet-Tieulent J, Curado MP, Ferlay J, Franceschi S, *et al*. Worldwide Trends in incidence rates for oral cavity and oropharyngeal cancers. *J Clin Oncol* 2013; 31(36): 4550-4559.

[5] Chaturvedi AK, Engels EA, Pfeiffer RM, Hernandez BY, Xiao W, Kim E, *et al*. Human Papillomavirus and Rising Oropharyngeal Cancer Incidence in the United States. *J Clin Oncol* 2011; 29(32): 4294-4301.

[6] Hong A, Lee CS, Jones D, Veillard AS, Zhang M, Zhang X, et al. Rising prevalence of human papillomavirus related oropharyngeal cancer in Australia over the last two decades. Head Neck 2015;38(5):743–50.

[7] Forte T, Niu J, Lockwood GA, Bryant HE. Incidence trends in head and neck cancers and human papillomavirus (HPV)-associated oropharyngeal cancer in Canada, 1992–2009. *Cancer Cause Control* 2012; 23(8): 1343-1348.

[8] Simard EP, Torre LA, Jemal A. International trends in head and neck cancer incidence rates: Differences by country, sex and anatomic site. *Oral Oncol* 2014; 50(5): 387-403.

[9] Winn DM *et al*. The INHANCE consortium: toward a better understanding of the causes and mechanisms of head and neck cancer. *Oral Dis* 2015; 21(6): 685-693.

[10] International Agency for Research on Cancer Working Group. IARC Monographs On The Evaluation Of Carcinogenic Risks To Humans: Human Papilomaviruses; 2007; Vol 90. http://monographs.iarc.fr/ENG/Monographs/vol90/ [Accessed: 5th April 2016]

[11] Hashibe M, Sturgis EM. Epidemiology of oral-cavity and oropharyngeal carcinomas: controlling a tobacco epidemic while a human papillomavirus epidemic emerges. *Otolaryng Clin N Am* 2013; 46(4): 507-20.

[12] Dahlstrom KR, Bell D, Hanby D, Li G, Wang L-E, Wei Q, *et al*. Socioeconomic characteristics of patients with oropharyngeal carcinoma according to tumor HPV status, patient smoking status, and sexual behavior. *Oral Oncol* 2015; 51(9): 832-838.

[13] Conway DI, Stockton DL, Warnakulasuriya K, Ogden G, Macpherson LMD. Incidence of oral and oropharyngeal cancer in United Kingdom (1990–1999)—recent trends and regional variation. *Oral Oncol* 2006; 42(6): 586-592.

[14] Carstairs, Vera, and Russell Morris. Deprivation and health in Scotland. *Health bulletin* 1990; 48(4): 162-175.

[15] Donnelley, R. Scottish Index of Multiple Deprivation 2009: general report. *Edinburgh, UK: Office of the Chief Statistician (The Scottish Government)* (2009).

[16] Waterhouse J, Muir, C.S.,Correa, P.,Powell, J., eds Cancer Incidence in Five Continents, Vol. III. *Lyon: IARC Scientific Publications*; 1976.

[17] Chaturvedi AK, Engels EA, Anderson WF, Gillison ML. Incidence Trends for Human Papillomavirus–Related and –Unrelated Oral Squamous Cell Carcinomas in the United States. *J Clin Oncol* 2008; 26(4): 612-619.

[18] Gillison ML, Broutian T, Pickard RK, Tong ZY, Xiao W, Kahle L, *et al.* Prevalence of oral HPV infection in the United States, 2009-2010. *Jama* 2012; 307(7): 693-703.

[19] Berkman LF, Macintyre S. The measurement of social class in health studies: old measures and new formulations. *IARC scientific publications* 1997(138):51-64.

[20] Macintyre S, Ellaway A. Ecological approaches: rediscovering the role of the physical and social environment. *Social epidemiology* 2000:332-348.
[21] Parkin DM, Bray F, Ferlay J, Pisani P. Global Cancer Statistics, 2002. *CA-Cancer J Clin* 2005; 55(2): 74-108.
[22] UK and Ireland Association of Cancer Registries, Performance indicators (Online). http://www.ukiacr.org/kpis [Accessed: 5th April 2016].
[23] Brewster D, Crichton J, Muir C. How accurate are Scottish cancer registration data? *Brit J Cancer* 1994; 70(5): 954-959.
[24] Brewster DH, Crichton J, Harvey JC, Dawson G. Completeness of case ascertainment in a Scottish regional cancer registry for the year 1992. *Public Health* 1997; 111(5): 339-343.
[25] Brewster DH, Stockton D, Harvey J, Mackay M. Reliability of cancer registration data in Scotland, 1997. *Eur J Cancer* 2002; 38(3): 414-417.
[26] Fischbacher CM. Identifying "Deprived Individuals": Are There Better Alternatives to the Scottish Index of Multiple Deprivation (SIMD) for Socioeconomic Targeting in Individually Based Programmes Addressing Health Inequalities in Scotland. Edinburgh, *UK: Scottish Public Health Organisation* 2014.