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Regional differences in incidence and mortality trends in cancers of the larynx, thyroid, oral cavity and pharynx in England and Scotland: 1975-2002

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ABSTRACT

Context: There have been significant changes in the epidemiology of head and neck cancers (HNC) in the last three decades worldwide. Documenting these trends helps to facilitate cancer prevention measures and aids resource allocation. Objective: To analyse incidence and mortality trends in Head and Neck Cancers (HNC) in the UK and compare regional differences between England and Scotland. Design: Retrospective quantitative analysis of time trends of HNC cases in the UK recorded in the International Agency for Research into Cancer (IARC) CI5 database and WHO mortality database. Setting: Cancer databases with extraction of UK HNC incidence and mortality time trends. Patients: All patients with cancers of the larynx, thyroid, oral cavity and pharynx in the UK (1975-2002) recorded in the IARC and WHO databases. Main Outcome Measures: HNC incidence and mortality trends in the UK. Results: There has been an increase in incidence of oral and pharyngeal cancer in the UK especially among males with higher rates in Scotland. However mortality has increased in Scotland and reduced in England. Thyroid cancer incidence has increased in the UK especially among females with higher rates in Scotland. Mortality has reduced in both regions. Laryngeal cancer among males has increased in incidence particularly in Scotland with a decline in incidence in England. Mortality has reduced significantly in England among males but increased in Scotland. Conclusions: In the UK, Scotland has higher incidence rates of HNC compared with England. Mortality has reduced in England from all the HNC sub-sites but has increased in Scotland for laryngeal, oral & pharynxgeal cancers. Although socioeconomic deprivation and its relation to higher alcohol and tobacco consumption have been highlighted as drivers, further studies are required.

Keywords: Head; Neck Cancers; Epidemiology; Thyroid; Laryngeal; Oral; Pharyngeal Cancers; UK; Incidence; Mortality

1. INTRODUCTION

There have been significant changes in the epidemiology of head and neck cancers (HNC) in the last three decades worldwide. This study analyses incidence and mortality trends in HNC in the UK and compares regional differences between England and Scotland. This will facilitate cancer prevention and resource allocation.

The head and neck cancer types included in this study are laryngeal, thyroid, oral and pharyngeal cancers. These cancers are the commonest HNC and demonstrated significant epidemiological trends in the period under review. Studies have reported increasing incidence of thyroid cancer in many countries in America and across Europe. In particular, differentiated thyroid cancers (papillary and follicular variants) have been shown to be on the increase. It is thought that may be due to increased diagnostic scrutiny with ultrasound scans picking up "incidentalomas". In some countries with a history of exposure to significant radiation such as the Chernobyl nuclear disaster, the incidence of thyroid cancers has justifiably increased.

Oral and pharyngeal cancers are also on the increase primarily due to exposure to the known risk factors of

alcohol consumption and cigarette smoking. There are regional differences seen across countries including the UK directly related to the degree of consumption of both alcohol and cigarettes. Higher rates of these cancers are found in countries with higher rates of exposure to these lifestyle risk factors. In recent decades, human papilloma virus has emerged as another significant driver for certain oropharyngeal cancers with an apparent epidemiologic and molecular difference compared to HPV negative tumours. There is still a lot not yet understood about HPV positive tumours but they appear to present in the younger age group and seem to respond better to treatment. Documenting these recent epidemiologic trends is crucial.

Laryngeal cancers on the other hand, are strongly associated with cigarette smoking and there has been a steady decline in laryngeal cancer incidence in England over the last 30 years that correlates with the falling rates of smoking. The experience in Scotland is different as there are higher rates of risk factor exposures with attendant mortality.

Studies have shown a strong correlation between socioeconomic factors and the development of cancers. There are regional differences between England and Scotland with some of the most deprived communities located in Scotland. This may be a contributory factor to the HNC rates although it is yet unproven and this study does not have that data to present.

We aim to present the changing time trends for each HNC sub-site with a view to directing resources and encouraging exploratory studies to explain the observed trends.

2. METHODS

2.1. Patients and Study Design

This is a retrospective quantitative analysis of time trends of HNC cases in England and Scotland recorded in the International Agency for Research into Cancer (IARC) CI5 database. Mortality trends were analysed from the WHO database.

Ethical approval was not required as the data is publicly available and provided by IARC. The data from IARC and the WHO was completely anonymised and as such there was no direct contact with any patients on the database. The IARC grants use of its data in the form provided and cited.

2.2. Statistical Analysis

Age-standardised incidence and mortality rates were recorded for England and Scotland over the study period by IARC. Using STATA, statistically significant trends were sought for each HNC sub-site in each country. Trend test for each graph was performed. A p-value less than 0.05 was deemed statistically significant.

3. RESULTS

3.1. Oral and Pharyngeal Cancer

Age-standardised incidence rates (ASIR) in Scotland for males rose from 8.35 per 100,000 in 1975 to 11.0 per 100,000 in 2002, $p < 0.001$ (**Figure 1**). In females, the rates also increased from 3.37 per 100,000 in 1975 to 5.04 per 100,000 in 2002, $p < 0.001$. Mortality increased significantly among males ($p < 0.001$) but not in females ($p = 0.19$).

In England, ASIR in males increased from 5.57 per 100,000 in 1985 to a peak 8.21 per 100,000 in 2001, $p < 0.001$ (**Figure 1**). In females, there was also an increase in ASIR from 2.91 per 100,000 in 1985 to a peak 3.82 per 100,000 in 2001, $p = 0.001$. Mortality reduced significantly among females ($p < 0.001$) but not in males ($p = 0.06$).

3.2. Thyroid Cancer

In Scotland, there was an increase in ASIR in females from 1.66 per 100,000 in 1975 to a peak 3.37 per 100,000 in 2001, $p < 0.001$ (**Figure 2**). In males, ASIR changed from 0.86 per 100,000 in 1976 to 0.97 per 100,000 in 2002, $p = 0.004$. Mortality reduced significantly among females ($p = 0.001$) with no change among males ($p = 0.25$).

In England, there was a significant increase in ASIR in females from 1.62 per 100,000 in 1985 to a peak 2.96 per 100,000 in 2002, $p < 0.001$. In males, there was a significant change in ASIR with 0.69 per 100,000 in 1985 to 0.89 per 100,000 in 2002 ($p = 0.001$). Mortality reduced among both males and females, $p < 0.001$ and $p = 0.01$ respectively.

3.3. Laryngeal Cancer:

In Scotland, there has been a significant increase in ASIR in males from 4.08 per 100,000 in 1975 to 6.67 per 100,000 in 2001 ($p < 0.001$). In females, ASIR was 1.16 per 100,000 in 1975 and 1.28 in 2002. Mortality increased from 1.96 per 100,000 in 1975 to 2.48 per 100,000 among males, $p = 0.001$ (**Figure 2**) with no change among females ($p = 0.16$).

In England, there has been a decline in ASIR for laryngeal cancer among males from 4.37 per 100,000 in 1985 to 3.85 per 100,000 in 2002, $p = 0.04$ (**Figure 1**). In females, there has been no change in ASIR with 0.79 per 100,000 in 1985 to 0.81 per 100,000 in 2002. Mortality reduced significantly among males from 1.80 per 100,000 in 1975 to 1.31 per 100,000 in 2002, $p < 0.001$ (**Figure 3**) and among females from 0.34 to

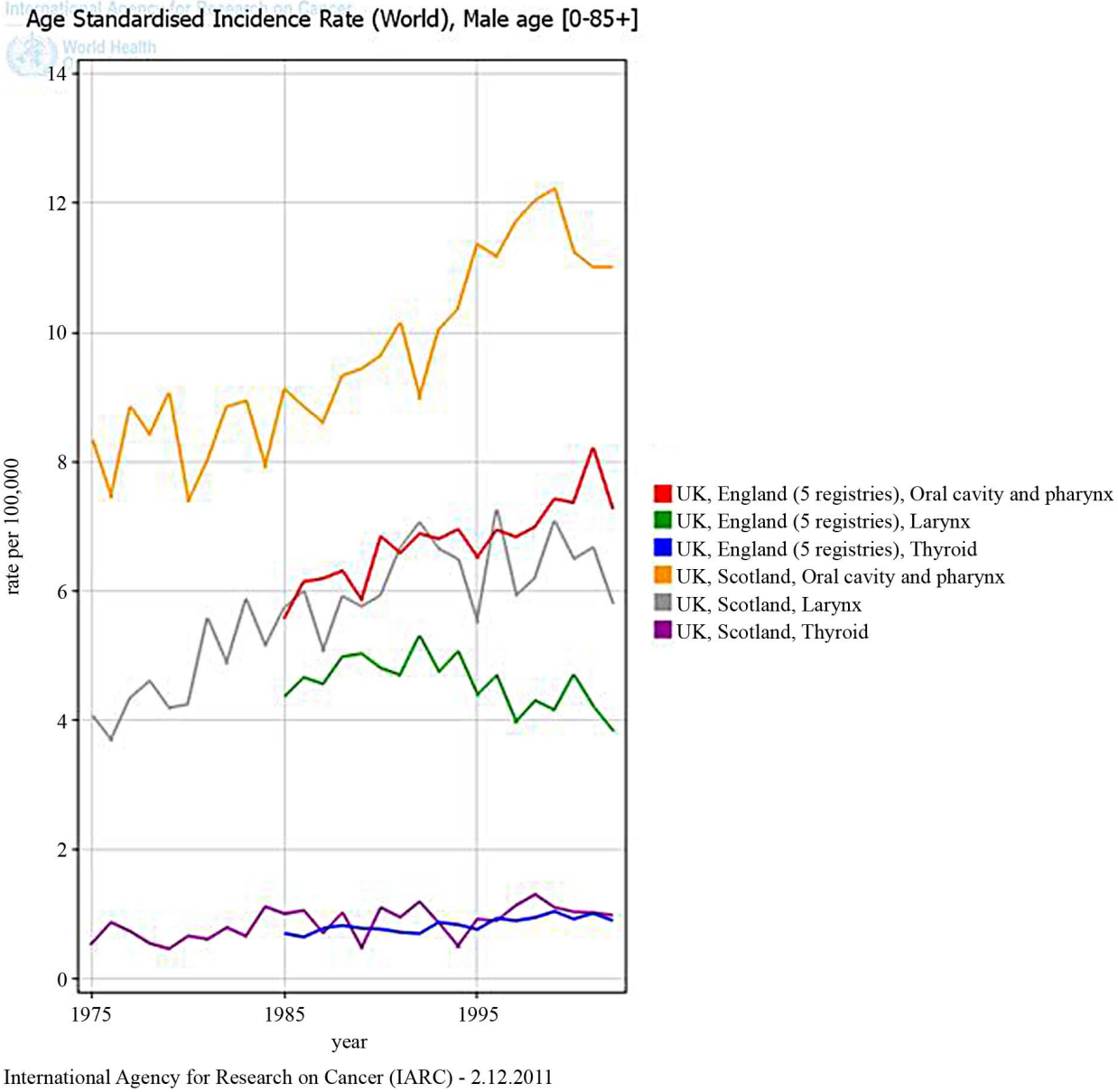

Figure 1. Age-standardised incidence rates in males in UK for cancers of the larynx, thyroid, oral cavity and pharynx.

to 0.24 per 100,000 $p < 0.001$ (**Figure 4**).

4. DISCUSSION

4.1. Thyroid Cancer

Thyroid cancer is the most common endocrine malignancy [1] and its incidence has increased over the last 30 years. Increasing incidence of differentiated thyroid cancer has been reported within USA, Europe and Canada [2].

Our study confirms worldwide trends and support recent published UK studies. Increased incidence in well-differentiated (papillary and follicular) histological types, in females and young adults within the South East of England between 1987-2006 have been previously highlighted [3,4]. Overall thyroid cancer increase between 1960-2002 in Scotland was noted to be primarily due to an increase in papillary cancer of all the histological subtypes with no significant change noted in the incidence of medullary and anaplastic thyroid cancer [3].

Improved detection and screening of smaller tumours (l - 2 cm), (since the wider use of ultrasound imaging in the early 1980s), and changes in clinical practice/histological criteria has been suggested to explain such rising trends.

SEER (Surveillance, Epidemiology and End Results) database analysis between 1998 and 2002 suggested that micropapillary thyroid cancer (<1 cm) accounted for

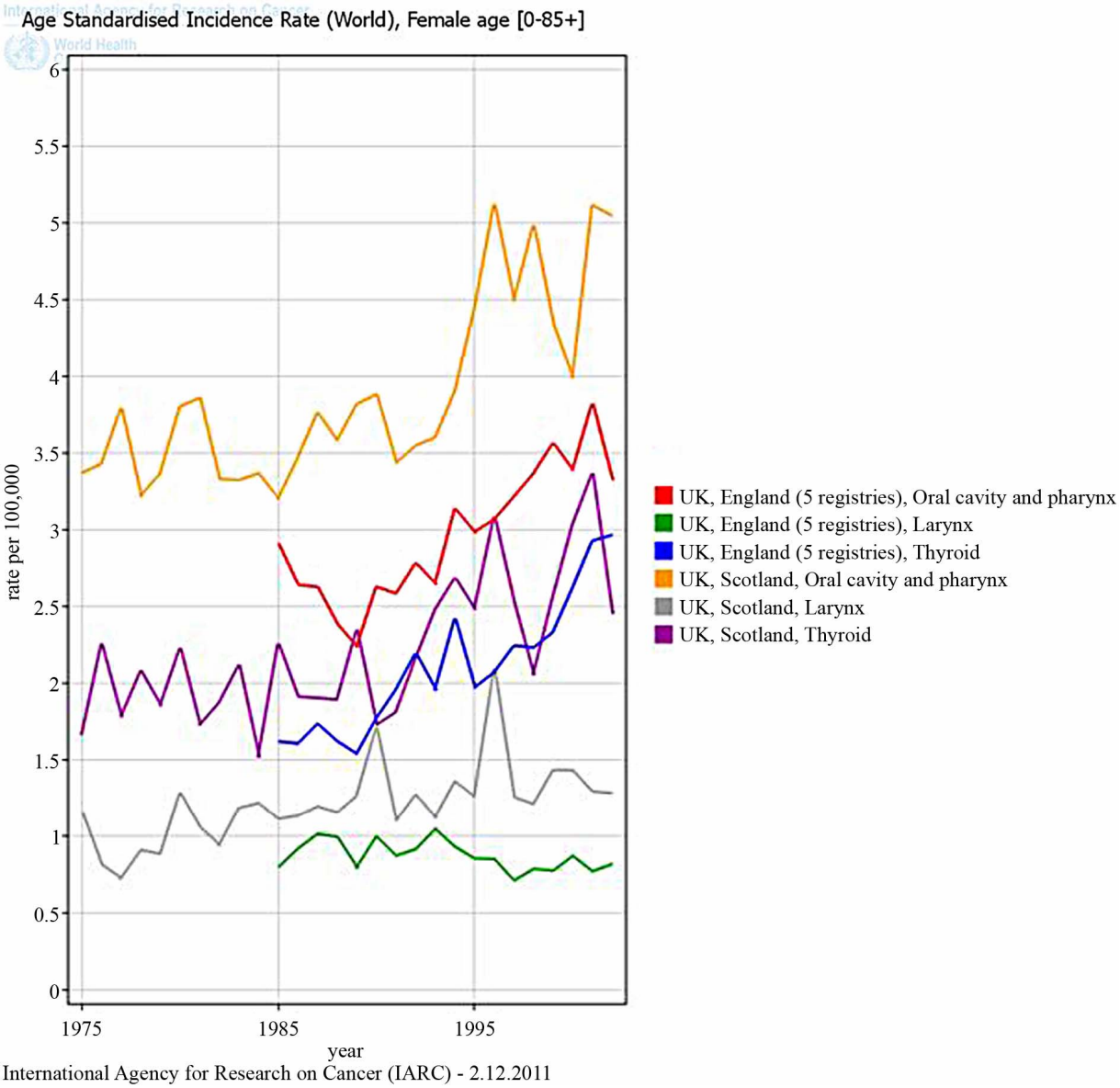

Figure 2. Age-standardised incidence rates in females in UK for cancers of the larynx, thyroid, oral cavity and pharynx.

49% of the overall increased incidence in thyroid cancer [5]. Furthermore, increased pathological reporting of micropapillary thyroid cancer in benign thyroid disease, on a background of evolving classification of histological criteria in thyroid malignancy over the last 30 years, has been suggested to explain current trends [5].

However, the theory that increased incidence rates reflects increased detection of subclinical disease, does not fully account for the greater rise in incidence in the developing world (where imaging remains limited) and the rise in detection of larger tumours (>2 cm) and more advanced thyroid cancer [1,6,7]. Further population-based studies based on the SEER database between 1973 and 2006, have shown incidence has more than doubled in well-differentiated thyroid cancers of palpable size (>2 cm) and larger (>4 cm and >6 cm) tumours [6].

Therefore, early detection or over-diagnosis does not fully account for the current rising trends and radiation exposure, hormonal, dietary/obesity, genetic or environmental risk factors have been suggested as possible areas of further investigation [1,6].

Radiation exposure, particularly in childhood, following nuclear fallout post nuclear weapon testing and Chernobyl has been identified as a cause in the development of thyroid cancer.

Limited studies exist to account for the disparity in thyroid cancer incidence rates in Scotland compared to England. An epidemiological study [8] within the UK focusing on trends during 1962 to 84 noted a peak in thyroid cancer risk in women born in the early 1950's,

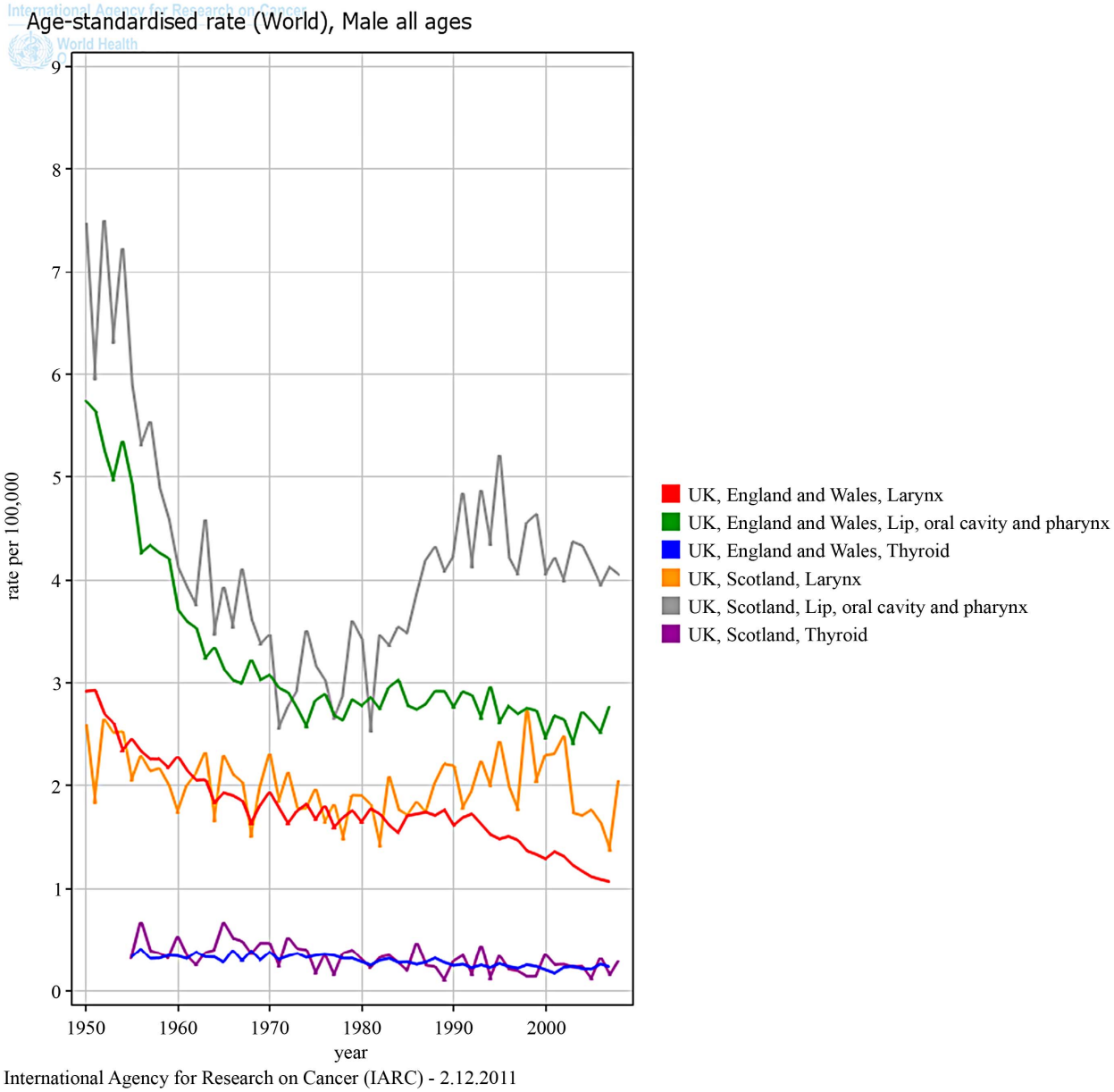

Figure 3. HNC mortality trends in males, UK.

when fallout radiation was greatest in England and Wales during nuclear weapon testing prior to the 1962 test ban treaty. Population-based data from the North of England in thyroid cancers in young people (<25 yrs) between 1968-1997 found a significant increase following the Chernobyl nuclear accident [9]. In particular, the increase in incidence was much greater in Cumbria.

An increasing BMI has been positively association with thyroid cancer risk [10]. Scotland has one of the highest levels of obesity (prevalence 25.5% 2003) amongst European countries, second only to the Unites States [11]. Furthermore women in Scotland are more likely to be obese than women in England with similar levels of obesity amongst Scottish and English men [11].

4.2. Laryngeal Cancer

Laryngeal cancer is the fourteenth most common cancer among males in England and Wales accounting for 1.4% of all cancers, whilst numbers of newly diagnosed cases and deaths in females are small [12]. Overall, age standardised incidence has fluctuated around 6 per 100,000 over the period 1971-1997, rising slightly in the late 1980s (congruent with smoking patterns) and subsequently declining. Smoking is the dominant risk factor for glottal cancers while alcohol is the major risk factor for cancers of the supra glottis. Over the last 30 years the use of tobacco in England has declined [13] which has been suggested as a possible contributory factor to the

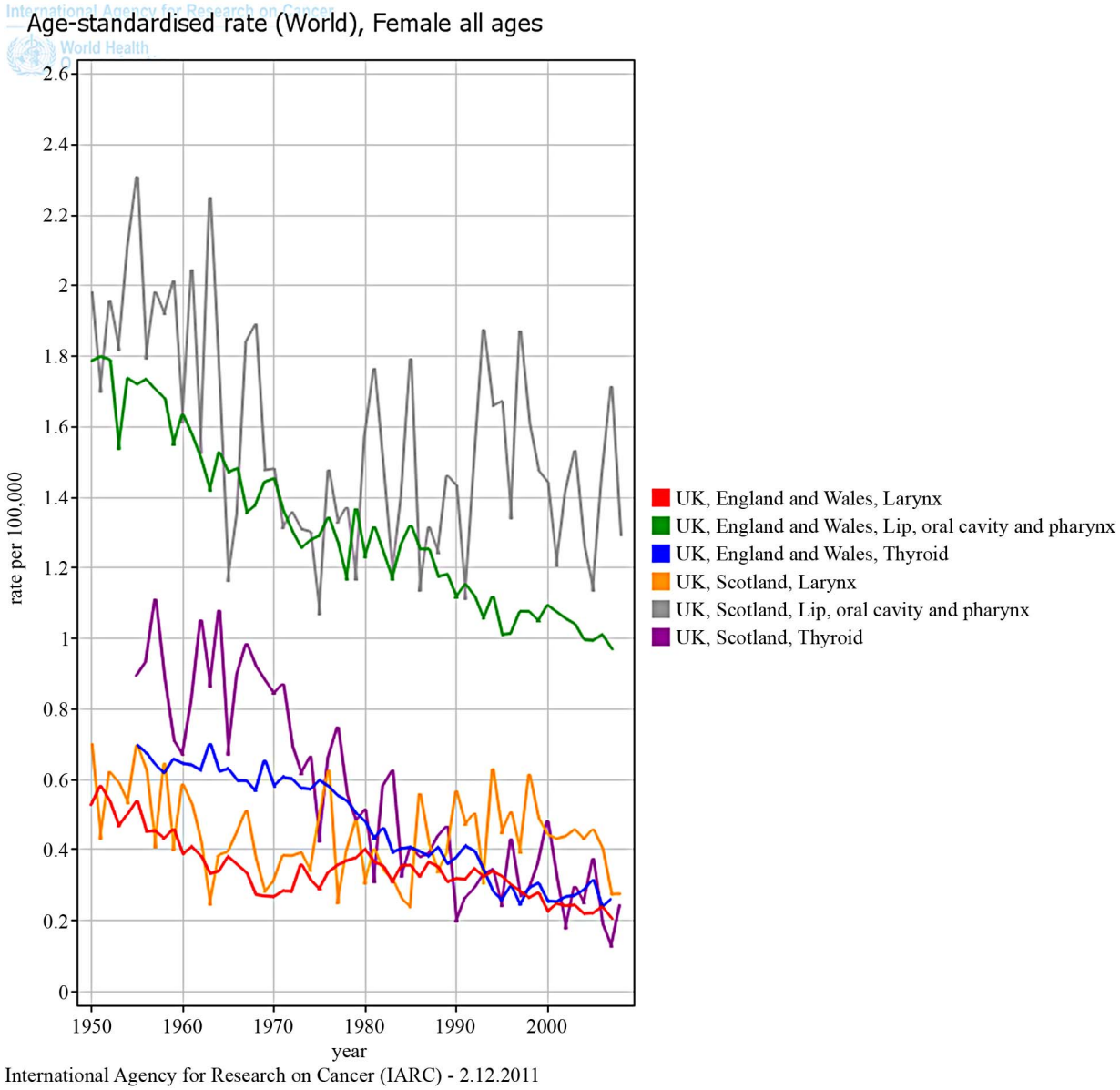

Figure 4. HNC Mortality trends in females, UK.

reduced incidence of head and neck cancers strongly associated with its use.

A recent study by Conway [14] on HNC risk factors used data from 15 case control studies enrolled on the International Head and Neck Cancer Epidemiology Consortium (INHANCE) with detailed information on cigarette smoking and alcohol consumption. Smoking risks were greater for cancers of the larynx than for the oral cavity or pharynx while alcohol risks were greater for cancers of the oral cavity and pharynx.

4.3. Oral & Pharyngeal Cancer

Oral and pharyngeal cancer is the sixth most common cancer in the world [15].

The incidence of oral cancer among young people in the UK has been increasing since the 1970s and age has been suggested to be a strong independent predictor of survival [16].

Increasing incidence of oral carcinoma among young patients has also been reported in Europe and the USA [17]. There have been previous reports of increasing incidence at young adult ages and mortality from oral, pharyngeal and laryngeal cancers in Scotland in both sexes [18,19].

Increasing alcohol consumption was associated with an increased risk of cancers of the oral cavity and pharynx in a study of over 1.2 million UK women [20]. Alcohol consumption is a recognised risk factor and this

has been shown to be associated with an increase in oral cavity cancers [21]. It must be noted however that alcohol is not an initiator of carcinogenesis, it is a promoter (or co-carcinogen)—therefore not an independent risk factor for head and neck squamous cell carcinoma, except at the highest levels.

Strong epidemiologic and laboratory evidence document an association between tonsil cancer and human papilloma virus [22-37] particularly in younger patients without the usual risk factors of alcohol or smoking. A recent systematic review and meta-analysis on HPV and head and neck squamous cell carcinoma in specific sites showed the strongest and most consistent association was for tonsil cancer, and the magnitude of this association was consistent with an infectious aetiology [23].

Within the UK, there has been a 51% increase in oral and oropharyngeal squamous cell carcinoma in men between 1989 and 2006, from 7 per 100,000 to 11 per 100,000 [38].

Oropharyngeal cancer has shown the greatest rate of increase of any cancer in Scotland. Although increased incidence was noted in all sub-sites, the greatest rise was noted for tonsil and base of tongue with a 2.9-fold increase in men compared to women [39]. Mortality from oral cancer has been on the decline in most Western European countries since the 1980s but there are persisting upward trends noted in Scotland alongside Belgium, Denmark, Greece and Portugal [40].

Different risk profiles have been identified with HPV positive HNSCC cancer versus HPV negative HNSCC [41], defining two distinct aetiological processes. HPV positive HNSCC has been associated with certain changes in patterns of sexual behaviour. One of the largest pooled analysis studies, noted an association of oropharyngeal cancer with a history of six or more lifetime partners, four or more lifetime oral sex partners and in men, an earlier age at first sexual intercourse [42]. A case-control study of 240 patients stratified by tumour HPV-16 status in HNSCC noted an independent association with increasing number of oral sex partners [36]. A recently published cross-sectional study (n = 5579) in the United States by Gillison *et al*. [43] found the prevalence of oral HPV was uncommon among sexually inexperienced individuals, was 8-fold higher amongst sexually experienced individuals and significantly increased with the number of sexual partners. Furthermore, oral HPV infection was approximately 3-fold higher in men than women, with the prevalence of HPV-16 more than 5-fold higher and a bimodal age pattern, with peak prevalence in individuals aged 30 - 34 years and 60 - 64 years was noted. The authors suggest that these findings may explain the rise of oropharyngeal cancer in younger individuals and in men.

In Great Britain, comparison between NATSAL I/II (The National Survey of Sexual Attitudes and Lifestyles) surveys carried out in the 1990 and 2000 respectively, have shown changing sexual behaviours [44]. In particular, an earlier age of first intercourse (median age 16yrs), an increase in the average number of lifetime partners, concurrent partners and oral/anal intercourse was shown.

From two large prospective head and neck cancer cohorts, patients in Scotland presented at a younger age and significantly more patients in Scotland had advanced stage III/IV laryngeal cancer [45]. In the West of Scotland, 5 year disease specific survival from oral and oropharyngeal cancer has been reported as 50% and overall survival as 35% with pathological nodal stage and perineural invasion identified as prognostic factors [46].

When considered by level of social deprivation, survival from cancers of the oral cavity and pharynx in Scotland is lower among persons from the most deprived areas, and it is among such persons that the recent increases in occurrence of cancers of the oral cavity and pharynx have primarily occurred [47].

4.4. Study Limitations

The study contained a large number of participants and includes three decades of data. This invariably could introduce bias given the size and the changes over time in collecting and analysing data. Further analysis is not possible as only aggregate data is available. There have also been changes in risk factor behaviour by region in the time interval and a number of improvements in HNC care including earlier diagnosis, improved referral pathways, better diagnostics and scans as well as better, less toxic treatments that have improved survival. This study takes that into consideration and only aims to provide time trends with an insight into the broad epidemiologic changes by HNC sub-site.

5. CONCLUSION

In the UK, Scotland had higher incidence rates for cancers of the larynx, thyroid, oral cavity and pharynx compared with England. Mortality has reduced in England from all the HNC sub-sites but has increased in Scotland for laryngeal, oral & pharyngeal cancers. Although socioeconomic deprivation and its relation to higher alcohol and tobacco consumption have been highlighted as drivers, further studies are required. The findings of this study will facilitate understanding of these regional differences in HNC epidemiology in the UK with a view to better identification of at-risk groups, and ensuring targeted cancer prevention and control measures.

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