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## Incidence and survival trends of head and neck squamous cell carcinoma in the Netherlands between 1989 and 2011



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#### SUMMARY

*Background:* Incidence and survival trends of head and neck squamous cell carcinoma (HNSCC) are essential knowledge for guiding policy making and research.

*Methods:* The total population of the Netherlands was studied covering 1989–2011. Two-and five-year survival and age-standardized incidence rates of HNSCC were assessed in relation to site, gender and age (15 years-of-age categories).

Results: We recorded a statistically significant increase of oral, oropharyngeal and hypopharyngeal carcinoma for males and females of all ages, varying from 0.6% (hypopharynx in males) to 2.7% (oropharynx in females) per year. The incidence of laryngeal carcinoma significantly decreased for males with 2.3% per year; for females the situation was stable. In young adults (below 45 years of age) the incidence figures were different: significant decreasing incidence trends were seen for both genders for carcinomas of the oropharynx, hypopharynx and larynx. Regarding oral carcinoma, no change was observed for the young patient group, but for subsites trends were divergent. Carcinoma of the floor or mouth decreased for both genders, but carcinoma of the tongue rose by a significant 2.8% per year for young males. Five-year survival trends for all ages showed no change for laryngeal carcinoma, a small improvement for oral and hypopharyngeal carcinoma, and a substantial and significant improvement of survival from 36% to 47% survival over the total period for oropharyngeal carcinoma.

Conclusion: In the Netherlands for the last two decades, the incidence of oral, oropharyngeal and hypopharyngeal squamous cell carcinoma has increased and survival has improved. The incidence of laryngeal carcinoma has decreased in males, and remained unchanged in females; survival from laryngeal carcinoma has not changed.

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#### Introduction

Head and neck cancer comprises malignancies arising in the upper respiratory and digestive tract and is a frequently occurring malignancy. Cancers of the oral cavity (including lip), pharynx (including nasopharynx) and larynx added up to a total number of approximately 690,000 new cases worldwide in the year 2012, which is 4.9 % of total cancer incidence [1]. Approximately, 375,000 people died from head and neck cancer worldwide in 2012, 4.6% of total cancer mortality [1]. Recent 2012 estimates for Europe showed 100,000 and 40,000 new cases for cancers of the oral cavity/pharynx and larynx, respectively [2].

It is impossible to generalize on recent incidence and mortality trends for head and neck cancer as there is variation by site, gender and geographical region. Looking at oral cavity cancer, a decrease of the age standardized incidence has been observed for the US [3] and Canada [4,5]. In Europe, increasing incidence trends have been reported for Portugal [6], Denmark [7], Italy (for females only) [8], France (for females only) [9], the South-East of England [10] and the Netherlands [11].

Oropharyngeal cancer is frequently reported to show an increasing incidence in Northern America and North-Western Europe. This has been described for the US [3], Canada [4], Scandinavia [7,12,13], France (for females only) [9], south-east England [10] and the Netherlands [11]. It is likely that the increase of oropharyngeal cancer must at least for a large part be contributed to the human papilloma virus (HPV) [14]. HPV-positive head and neck squamous cell carcinoma (HNSCC) must be considered a separate group of tumors, with a unique genetic profile [15,16] and a better prognosis [17,18].

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A worrying finding in the literature is the increasing incidence of oral cancer in younger age groups, reported for the US [19,20], Scandinavia [21], United Kingdom, Switzerland and Slovakia [22].

Recent studies report an improvement of the five-year survival rates in the more developed countries. In the US, the comparison of time periods 1992–1996 and 2002–2006 gave improved five-years survival rates, that varied from 1.9% for patients with larynx cancer to 23.2% for tonsil cancer [23]. In most European countries there was an improved 5-years survival for patients suffering from oral/oropharyngeal cancer during the period from 1990 to 2002 [24]. Survival trends of patients with laryngeal cancer are variable per country, though in most countries a slight improvement is observed [24].

We previously published incidence trends of head and neck cancer, in particular on HNSCC in the Netherlands covering the period 1989–2006 [11]. A statistically significant rise of HNSCC of the oral cavity (females) and oropharynx (males and females) was reported, contrasting with a decline of laryngeal cancer for males. The incidence of HNSCC in the younger age group did not show an increasing trend [11].

The present study highlights more recent data on incidence trends of HNSCC in the Netherlands covering the longer period 1989–2011, taking age and subsite into account. In addition, survival trends of this period are reported herein.

#### Materials and methods

Data were obtained from the Netherlands Cancer Registry covering the period 1989-2011. This dataset approximates the total Dutch population, that rose from 14.8 million in 1989 to 16.6 million in 2011. Only squamous cell carcinomas (SCC) from the head and neck region were included: oral cavity, oro- and hypopharynx and larynx. Subsite coding was according to the ICD-O-3 classification [25], while subsite grouping was according to Sobin et al. [26]. The oral cavity was divided in buccal mucosa (ICD-O topography codes C00.3, C00.4, C06), upper alveolus and gingiva (C03.0), lower alveolus and gingiva (C03.1), hard palate (C05.0), oral tongue (C02) and floor of mouth (C04). The oropharynx was divided in anterior wall (base of tongue [C01] and vallecula [C10.0]), lateral wall (C10.2, including tonsil C09), posterior wall (C10.3), superior wall (soft palate, C05.1 and uvula, C05.2) and remaining or unspecified parts (C10.4, C10.8, C10.9). The hypopharynx was categorized as postcricoid area (C13.0), piriform sinus (C12.9), posterior hypopharyngeal wall (C13.2) and remaining or unspecified parts (C13.8, C13.9). Finally, the larynx was included with three subsites: supraglottis (C32.1, C10.1), glottis (C32.0) and subglottis (C32.2). As a result of the restriction to SCC, 5.5% (oral cavity 6.6%; oropharynx 5.8%; hypopharynx 4.5%; larynx 2.2%) of all tumors were excluded because of the following reasons: adenocarcinoma (2.7%), undifferentiated carcinoma (0.9%), neuroendocrine carcinoma (0.3%) and other and unspecified cancers (0.7%). Carcinomas of the lip (C00), nasopharynx (C11), nasal cavity (C30.0) and sinuses (C31.0 and C31.1) were not included, because of other etiological factors (lip and nasopharynx) and low numbers (sinuses). Stage classification was according to the TNM classification [26].

Incidence data were expressed as ESR, the European age-standardized rate per 100,000 inhabitants. Besides, incidence was calculated for four age groups: below 45, 45–59, 60–74 and over 75 years of age. Estimated annual percentage change (EAPC) of the incidence rates was calculated by log-linear regression. The trend was considered to be significant, when the *p*-value was below 0.05. Two and five year relative survival rates (RSR) were calculated for different calendar time cohorts. We estimated relative survival as the ratio of the observed survival to the expected survival in the general population of the same age and gender, according to Dickman et al. [27].

#### Results

Incidence trends for the four main sites of HNSCC in the period 1989–2011 are shown for both genders in Fig. 1. The EAPC of the main sites, but also of the subsites, are shown in Table 1 (all ages and individuals below 45 years) and Supplementary Table 1 (all age-groups). Two- and five-years RSR are listed in Table 2.

#### HNSCC grouped from all sites

The incidence from 1989–2011 showed a statistically significant decreasing trend of 0.4% per year for males (Table 1). In contrast, there was an increase of 1.7% per year (p < 0.05) in females. Tumor site considerably influenced the gender distribution; the male to female ratio was lowest for oral cavity (1.4) and highest for the larynx (4.4) (Table 1, the period 2007–2011). The incidence rate of HNSCC in young adults decreased significantly with 1.8% per year for both genders. The five-year RSR did not show an overall change for all age groups, despite positive effects for some tumor sites (detailed below, Table 2). Two-year RSR appeared to improve, judged from the statistical difference between the first and last time-cohorts. Distribution of disease stages was quite constant during the total study period (Supplementary Table 2).

#### Oral cavity

The incidence of SCC of the oral cavity has significantly increased during the past 23 years, with 0.7% and 1.8% per year in males and females, respectively (Table 1, Fig. 1). A statistically significant increase was seen for most subsites, with a stable situation for floor of mouth in both genders, buccal mucosa in males and hard palate in females (Table 1). In young adults (below 45 years) the oral carcinoma incidence did not change significantly over time (Table 1). There were, however, divergent results according to subsite. Tongue carcinoma showed an increasing trend in both genders, and for males this increase was statistically significant. This is in contrast with tumors of the floor of mouth, for which a statistically significant decrease was observed for both genders. Also the incidence of carcinoma of the lower alveolus and gingiva has significantly decreased in young males.

A moderate improvement of the 5-year RSR (all ages) was recorded for oral cavity SCC, from 56% (95% confidence interval [CI] 54–58%) for cases diagnosed in 1989–94 to 62% (95% CI 60–64%) in 2007–11 (Table 2).

#### Oropharynx

Of all head and neck sites, SCC of the oropharynx shows the highest level of increase in incidence. A significant 2.1% and 2.7% increase per year was observed for males and females, respectively (Table 1). An increase was observed for all subsites of the oropharynx, with only small differences in EAPC per subsite. In contrast to the trend for all age groups combined, a significantly decreasing trend was observed for young adults of both genders (Table 1).

Five-year RSR showed a consistent increase in the study period and went from 36% (95% CI 33–39%) in 1989–1994 to 48% (95% CI 45–50%) in 2007–2011 (Table 2).

#### Hypopharynx

The incidence of hypopharyngeal SCC has increased during the past 23 years (Table 1). EAPC were significantly positive for males

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