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Mouth Cancer for Clinicians Part 2: Epidemiology

Abstract: A MEDLINE search early in 2015 revealed more than 250,000 papers on head and neck cancer; over 100,000 on oral cancer; and over 60,000 on mouth cancer. Not all publications contain robust evidence. We endeavour to encapsulate the most important of the latest information and advances now employed in practice, in a form comprehensible to healthcare workers, patients and their carers. This series offers the primary care dental team, in particular, an overview of the aetiopathogenesis, prevention, diagnosis and multidisciplinary care of mouth cancer, the functional and psychosocial implications, and minimization of the impact on the quality of life of patient and family.

Clinical Relevance: This article offers the dental team an overview of the changing epidemiology of, and increases in, mouth cancer.

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About 2 out of every 100 cancers diagnosed (2%) are mouth cancers (oral and oropharyngeal) and these are the most common head and neck cancers. Mouth cancers are mainly oral squamous cell carcinomas (OSCCs). Cancers can arise in any part of the mouth, but especially the lip, tongue and oropharynx (OPSCC or OPC). Cancer of the lip accounts for around 6% of cases. The most common cancers are in the mouth, mainly on the side of the tongue, collectively accounting for 60% of cases in 2010. Cancers of the 'oral cavity and oropharynx' are classified in the ICD

(International Classification of Diseases) and include cancers of the lip, tongue and mouth (oral cavity) [ICD-10: C00-06] and oropharynx [ICD-10: C09-C10] (Article 1).

Oral and oropharyngeal cancers, though not common, are more common than cancers of:

- Bone;
- Brain;
- Cervix;
- Hodgkin lymphoma;
- Liver;
- Ovaries;
- Stomach;
- Thyroid.

estimated that there were almost 900,000 patients with cancers of the lip, oral cavity and pharynx (excluding the nasopharynx) still alive up to 5 years after their diagnosis. OSCC was the eleventh most common cancer, accounting for an estimated 263,000 new incident cases and 127,700 deaths annually. Worldwide, approximately 500,000 new cases of head and neck cancer are diagnosed annually.

Internationally, three-quarters of cases of mouth cancer affect people from the resource-poor, developing world. Oral cancer continues to be a major cancer in the Indian subcontinent where the incidence rate approaches 50% of all cancers (male incidence rates up to 6.5 per 100,000 per annum). East Asia, eastern Europe, and Latin America and migrants from these areas are also risk groups.

Resource-poor populations

Mouth cancer is particularly common in people from the developing world. Oral and pharyngeal cancers rank in the top three in high incidence areas. There is a wide geographical variation but two-thirds of the cases occur in people from South Asia (including Sri Lanka, India,

What is the size of the mouth cancer problem?

Oral and oropharyngeal cancers together are the sixth leading cancer in the world, with a wide geographical variation, although two-thirds of the cases occur in resource-poor countries, such as countries in South Asia, Latin America and Papua New Guinea and some pacific islands. The incidence rates in Europe are higher in eastern compared with western, northern or southern Europe.

Worldwide, in 2008, it was

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Pakistan, Taiwan); Latin America (Brazil, Uruguay, Puerto Rico and Cuba); and Papua New Guinea and other pacific islands in Melanesia. In certain countries, such as Sri Lanka, India, Pakistan and Bangladesh, oral cancer is the most common cancer recorded. In parts of India, oral cancer can represent more than 50% of all cancers. Unfortunately, some parts of the world where oral cancer is most common are also those where descriptive information (ie incidence, mortality, prevalence) is least available or robust.

Primary cancers of the *nasopharynx* are distinct among head and neck cancers in aetiology and in racial and geographic distribution – endemic to southern China, south-east Asia and northern Africa, and its pathogenesis is thought to involve exposure to nitrosamines from salted fish consumption, and to viruses infecting the upper aerodigestive tract – particularly Epstein-Barr virus (EBV).

Resource-rich populations

OSCC is the eighth most common form of cancer overall in people in developed countries, although the ranking varies a great deal among countries. The incidence in developed countries is generally higher in ethnic minorities and immigrants from high risk areas.

USA

In 2008 in the USA, head and neck cancer was diagnosed in an estimated 35,000 people, accounting for 3% of all new malignancies. In 2013, the figure had risen to around 36,000. Males were at higher risk, with significant racial and socioeconomic disparities in disease incidence. In particular, African-Americans have a higher incidence, more advanced disease at presentation, and generally greater mortality when compared to White Caucasians.

Europe

Estimates show that more than 32,000 new cases of oral cancer are diagnosed annually throughout the European community. The incidence rates are higher in eastern compared with western, northern or southern Europe. Within the European Union (EU), the highest

male incidence rates within the 27 EU countries are in Hungary, Slovakia, Slovenia and France. For example, in areas of northern France, OSCC is the most common form of cancer in men.

In 2008, the highest European age-standardized (AS) incidence rates were estimated to be in Hungary for men (22 cases per 100,000) and The Netherlands, Denmark and Hungary for women (around 5 cases per 100,000), while the lowest rates were in Cyprus and Greece for men (around 3 cases per 100,000) and Romania for women (1 per 100,000).

UK

Mouth cancer is a growing problem in the UK, with high relative mortality and increasing incidence; rates in the UK have risen by a third in the last decade, with 6500 cases diagnosed in 2010. For 2013, it was expected that there would be over 7,500 new mouth cancer cases in the UK. Cancer of the lip, however, is uncommon in the UK, with around 340 people diagnosed with it each year.

Further details are available from Table 1, Figure 1 and Further Reading.

Across the UK there is a north-



Figure 1. Cancer Research UK statistics. (Courtesy of CRUK.)

Body	Acronym	URL
British Association of Head and Neck Oncologists	BAHNO	http://www.bahno.org.uk/
Cochrane Collaboration	Cochrane	http://www.cochrane.org/reviews/en/subtopics/84.html
Cancer Research UK	CRUK	http://www.openuptomouthcancer.org/index.htm
National Institute of Health and Clinical Excellence	NICE	http://www.nice.org.uk/Guidance/CSGHN
National Institutes for Dental and Craniofacial Research	NIDCR	http://www.nidcr.nih.gov/oralhealth/topics/oralcancer/detectingoralcancer.htm

Table 1. OSCC: various bodies in UK/USA providing information.

south divide (particularly for males). The latest analysis of oral cavity cancer (ICD-10 C02-C04, C06) incidence rates showed that the highest incidence rates are still in Scotland, Northern Ireland and the north of England. In the UK, incidence rates are also high among South Asian women and in recent/new migrants from eastern EU. The age-standardized (AS) rates for oral cancer are significantly higher in Scotland compared with the other constituent countries of the UK for males, and compared with England and Wales only for females. The rates do not differ significantly between England, Wales and Northern Ireland for either gender.

The geographical variation in oral incidence appears largely to reflect the prevalence of exposure to well-established risk factors – tobacco and alcohol (Article 4).

How is the epidemiology of mouth cancer changing?

The number of cases of mouth cancer is rising in many countries. The prevalence of intra-oral cancer appears to be rising, especially in younger people: more than one in ten cases is now diagnosed in people below the age of 50. There is concern about this ongoing increase in younger patients and in women.

USA

Oral cancer rates still increase with patient age; the increase becomes more rapid after the age of 50 and peaks between ages 60 and 70. Oral cancer rates are significantly higher for males than for females and are higher for Hispanic and Black males than for White males.

Oral cancer rates have increased approximately 15% from the mid-1970s until the latest (2004) National Cancer Institute Survey. In 2008 in the USA, head and neck cancer was diagnosed in an estimated 35,000 people, accounting for 3% of all new malignancies. Current American Cancer Society estimates indicate that, in 2013, approximately 36,000 people were diagnosed with oral cavity and oropharyngeal cancers, with an estimated 6850 of those diagnosed dying from their cancers.

HPV exposure and infection increase the risk of oropharyngeal cancer independently of tobacco and alcohol use. Between 1973 and 2009, there was a 60% overall increase in oropharyngeal cancer in people under 45. Among Caucasians, the increase was 113%, but the rate of such cancers declined by 52% in African-Americans. However, the five-year survival rate remained worse for African-American patients.

Europe

From 1999–2001 and 2008–2010, the European AS oral cancer incidence rates have increased by 26% and 30% in males and females, respectively.

European AS incidence rates for males from 1975–1977 and 2008–2010 increased by 76%. The largest increases in males have been in those aged between 50 and 59, with European AS incidence rates almost tripling (189%) from 1975–1977 and 2008–2010. The rise was similar for females, with rates increasing by 83% from 1975–1977 and 2008–2010. For females, the largest increases have been in those aged below 49, where rates more than doubled (122%) from 1975–1977 and 2008–2010.

UK

In the UK, since the mid-1970s, incidence rates of mouth cancer have increased overall for all of the broad age groups, except males aged 80+. In 1984, 3,030 people were diagnosed with mouth cancer. Since the 1980s, there was an overall decline in diagnoses of new head and neck cancers attributed to public health efforts against tobacco use but, since the 1990s, cases of oral cancer increased by nearly 30% for men in their forties and by nearly 25% for women. From 1971–2003 the incidence of oral cancer trebled, with a steeper increase more recently. This is continuing, with the age-standardized three-year average incidence rate rising by over 20% when comparing years 1997–1999 with 2006–2008. The 2006–2008 incidence in males was 12.7/100,000 and 5.6/100,000 in females. By 2007, the UK incidence figures (per 100,000 population) were:

- All oral cavity cancers: 7.6 (males 10.9; females 4.6);
- Mouth: 2.3 (males 3.0; females 1.6);
- Tongue: 2.3 (males 3.2; females 1.5);
- Lip: 0.3 (males 0.5; females 0.2).

In 2009, there were 6,240 new cases of oral cancer in the UK. In 2010, there were 6,539 new cases: 4,307 (66%) in men and 2,232 (34%) in women, giving a male:female ratio of more than 19:10. Mouth cancer in 2010 was the 15th most common cancer, accounting for 2% of all new cases. In males, it was the 11th (3% of the male total), and in females the 15th (1%) most common. In 2010, there were 1,985 mouth cancer deaths reported. In 2011,

around 6,800 people were diagnosed with oral cancer – more than 18 people every day. There are now about 14 new oral cancer cases for every 100,000 males in the UK, and 7 for every 100,000 females. By 2030, it is predicted that there will be 9,200 cases of oral cancer in the UK every year.

Summary

Rates of mouth cancer continue to rise in both men and women and in all age groups, including the under 50s, with more young people developing mouth cancer than ever before. The prevalence of lip cancer, in contrast, appears to be decreasing in the UK.

The number of people being diagnosed with mouth cancer is increasing, with notable rises in incidence in females and in younger people. Although rates of mouth cancer have traditionally been higher in men than in women, this gap is narrowing over time; the ratio of males to females diagnosed with oral cancer has declined and is now about 1.5:1 for the mouth and about 2.8:1 for cancer of the oropharynx.

There may be several reasons for these changes, including the ageing population, changing demographics and changing lifestyles, such as the past changes in the prevalence of major risk factors, including heavy smoking and alcohol consumption, and now increased infection with the human papilloma virus (HPV) as a consequence of changing behaviours. Oral cancer is also seen more frequently in the UK in Asians, particularly in Bangladeshi men, and the racial/ethnic disparity in oral cancer rates in the world is largely attributable to lifestyles, particularly chewing tobacco and areca nut, and the use of waterpipes (Articles 3, 4 and 5).

Nevertheless, although there has been a significant increase in patients with mouth cancer in the UK under the age of 45 over the last 20 years, mouth cancer is still predominantly a disease of older patients. The mouth cancer burden falls heavily on lower socio-economic groups, with incidence rates around 130% higher in men in deprived areas compared to the least deprived and more than 74% higher in women.

Is mouth cancer survival changing?

The death rate from oral cancer is higher than that of many cancers, such as cervical cancer or malignant melanoma. The best outcomes for overall five-year survival rates for treated mouth cancers are for cancer of the lip, at over 90% of patients. This relates presumably to the very early diagnosis at this easily visualized site.

The survival at five years from mouth cancer diagnosis was for many decades about 50%, but over the last ten years approaches 60%. For most countries, five-year survival rates for treated oral cancers of the tongue, oral cavity and oropharynx are currently around 50–60%.

Survival rates for individual mouth cancers vary, but those who will live for five years or more include:

- Lip cancer – nearly 90 out of 100 people diagnosed (89%);
- Oral cavity (all other mouth cancers) – nearly 55 out of every 100 women (55%) and 48 out of every 100 men (48%);
- Tongue cancer – 55 out of 100 women (55%) and 44 out of 100 men (44%).

The modest improvement in overall survival is probably due to advances in treatment and rehabilitation. Overall, Black and White patients appear to have similar outcomes for most head and neck cancer sites when they receive the same high-quality care.

In general, prognosis decreases with advanced disease, low socio-economic status (SES), advanced age and continuing risky lifestyles. Generally speaking, the earlier a cancer is found and treated, the better the outcome is likely to be. Mouth cancer is a major neoplasm worldwide and theoretically should be largely preventable or detectable at an early stage. However, patients frequently delay seeking professional advice on average for periods up to three months after having become aware of any oral symptom that could be linked to mouth cancer (Article 7). Delays during the referral and treatment processes are now short (Articles 6 and 7).

During the first five years following successful therapy for oral and oropharyngeal cancer, patients need regular surveillance to detect any recurrences. Also, in 20–30% of patients, second primary cancers of head and neck may arise for up to 20 years due to clonal evolution.

Cancer survivors have special long-term needs, both physical and psychological (Article 13).

What are the known risk groups for mouth cancer?

Factors important in mouth cancer aetiology include, especially, lifestyle modifiable risk factors, such as tobacco (discussed in Articles 3 and 4 mainly) and:

- Age: mouth cancer is more common in people over 45, although an increasing number of young people are developing the condition, especially women.
- Gender: mouth cancer is generally more common in men than women, attributable to heavier indulgence in risk habits (tobacco and alcohol) by men and exposure to sunlight (for lip cancer) as a part of outdoor occupations. Fifty years ago, mouth cancer was five times more common in men but now it is only twice as common as in women.
- Social class: mouth cancer is a problem particularly of people of lower socioeconomic status (SES), especially in males.

The traditional risk groups for oral cancer remain older males who have habits such as tobacco, alcohol or betel use, but increasingly oropharyngeal cancers are seen in younger people of either gender and related to viruses such as HPV.

It is dangerous not to consider a diagnosis of cancer just because a patient is not in a 'risk group'.

Further reading

1. http://www.ncin.org.uk/cancer_type_and_topic_specific_work/cancer_type_specific_work/head_and_neck_cancers/head_and_neck_cancer_hub/profiles
2. <http://www.cancerresearchuk.org/cancer-info/cancerstats/types/oral/incidence/uk-oral-cancer-incidence-statistics>
3. <http://www.oralcancerfoundation.org/facts/#sthash.tp5770od.dpuf>
4. <http://www.isdscotland.org/Health-Topics/Cancer/Publications/index.asp>
5. <http://www.ons.gov.uk/ons/rel/vsob1/cancer-statistics-registrations--england--series-mb1-/index.html>
6. <http://www.qub.ac.uk/research->

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