



Review

Global epidemiology of oral and oropharyngeal cancer

Saman Warnakulasuriya *

Department of Oral Medicine and Experimental Oral Pathology, King's College Dental Institute, Bessemer Road, London SE5 9RS, UK
 WHO Collaborating Centre for Oral Cancer and Precancer in the United Kingdom, Denmark Hill Campus, London SE5 9RS, UK

ARTICLE INFO

Keywords:
 Oral cancer
 Epidemiology
 Incidence
 Mortality

SUMMARY

This review presents data on incidence, mortality, survival and trends in cancers of the lip, oral cavity and oropharynx using available recent data sources around the world. Oral and pharyngeal cancer, grouped together, is the sixth most common cancer in the world. The review focuses primarily on several high-risk countries in an attempt to gain insight into the geographic variations in the incidence of this cancer in the globe and to relate the high incidence in some populations to their life style. With an estimated half a million cases around the globe and the rising trends reported in some populations, particularly in the young, urgent public health measures are needed to reduce the incidence and mortality of oral and oropharyngeal cancer.

© 2008 Elsevier Ltd. All rights reserved.

Introduction

This review on 'oral and oropharyngeal cancer' describes the global epidemiology of cancers of the lip, tongue and mouth (oral cavity) [ICD-10: C00-06], and oropharynx [ICD-10: C09-C10], excluding the salivary glands [C07-08] and other pharyngeal sites [C11-13]. In some world reports, cancers of all sites of the oral cavity and pharynx are grouped together [ICD-10: C00-14], and these are cited in the review as they are originally described. More than 90% of oral malignancies in the upper aerodigestive tract are squamous cell carcinomas. The large majority of oral cancers have risk factors similar to those occurring in the rest of the head and neck or the upper aerodigestive tract. Most cancers of lip and oral cavity are preventable.

Global incidence

Oral cancer is a serious and growing problem in many parts of the globe. Oral and pharyngeal cancer, grouped together, is the sixth most common cancer in the world. The annual estimated incidence¹ is around 275,000 for oral and 130,300 for pharyngeal cancers excluding nasopharynx, two-thirds of these cases occurring in developing countries. There is a wide geographical variation (approximately 20-fold) in the incidence of this cancer. The areas characterised by high incidence rates for oral cancer (excluding lip) are found in the South and Southeast Asia (e.g. Sri Lanka, India, Pakistan and Taiwan), parts of Western (e.g. France) and Eastern Europe (e.g. Hungary, Slovakia and Slovenia), parts of Latin America and the Caribbean (e.g. Brazil, Uruguay and Puerto Rico) and in Pacific re-

gions (e.g. Papua New Guinea and Melanesia) (Fig. 1). Data illustrated in Figure 2 are based on cancer incidence in five continents (ninth volume)², which has become the recognised reference source on the incidence of cancer in populations around the world presenting data for around the year 2000 (covering the period 1998–2002). Scanning through the information, it was possible to extract data either for entire populations or for sub-populations living in some geographic areas. For some countries with several data sets from several regions, two highest rates for the population are extracted and shown in Figure 2.

In high-risk countries such as Sri Lanka, India, Pakistan and Bangladesh, oral cancer is the most common cancer in men, and may contribute up to 25% of all new cases of cancer. On a visit to a cancer treatment centre in any of these high-risk countries in south Asia, one may find that at least up to a quarter of the patients warded are suffering from oral cancer.

European Union and Eastern European countries

In 2004, there were 67,000 new cases registered in the countries of the European Union (EU). Overall in the EU, oral and pharyngeal cancer occupies the 7th position.³ Within the EU countries the highest male incidence rates are found in France and Hungary, and the lowest rates are found in Greece and Cyprus. In one report the rate for oral cancer in men in France was almost seven times greater than that for men in Greece.⁴ The lifetime risk of developing oral and pharyngeal cancer in Europeans is estimated at 1.85% for men and 0.37% for women. The incidence rates are higher in Western Europe compared with Northern or Southern Europe. Highest mortality rates, however, are reported from Eastern Europe. A comparison of incidence and mortality rates among Europeans is shown in Figure 3.

* Tel.: +44 20 3 299 2430; fax: +44 20 3 299 3426.
 E-mail address: s.warne@kcl.ac.uk

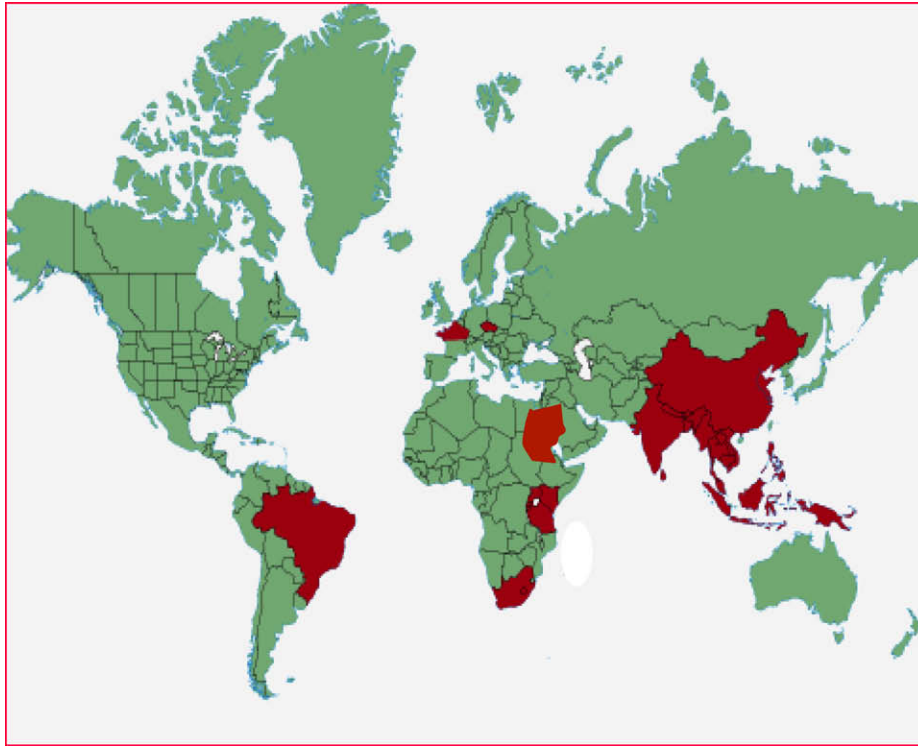


Figure 1. Countries with high incidence and mortality from oral cancer.

Within the European Union, France has the highest incidence rates and in the recent years around 15,500 cancers of lip, oral cavity and pharynx were reported annually. This amounts to 5.5% of cancer incidence in the country. The reported incidence rates in France were 32.2 (males) and 4.7 (females) per 100,000 (standardised to European populations).⁵ The incidence of both oral and oropharyngeal cancers among males is extremely high in northern France with a rate of almost 42.3 per 100,000 among men in the Somme and Bas Rhin regions. **Figure 3** illustrates a comparison of rates in Europe, with France having the highest incidence. About 5000 deaths are reported per year.

Spain, Portugal, Germany, Switzerland and northern regions of Italy have reported intermediate rates compared with other countries of Europe.

In the United Kingdom (UK) oral cancers are not common. There were 4660 new cases of oral and pharyngeal cancer diagnosed in 2003 and accounted for 1.6% of all new cancers, outnumbering cervical cancer, ovarian cancer and leukaemia.⁶ The disease is on the increase in young adults and most UK cancer registries record 6% of all oral cancers in young people under the age of 45 years. Rates in Scotland are higher than in other parts of the UK for both men and women. The lifetime risk of developing oral cancer is considerably higher in Scotland (1.84% in males and 0.74% in females) than the rest of the UK (1.06% and 0.48%, respectively, for UK as a whole).⁷

Lowest incidence rates within Europe are in Greece, Finland and Sweden.

In the recent decades, several Central and Eastern European countries, e.g. Hungary, Slovakia and Slovenia, have reported high rates for oral cancer. This is particularly true for Hungary where incidence and mortality have doubled and the projected increases represent the most serious situation in Europe.⁸

United States of America

Approximately 34,360 cases of oral cancer and pharynx cancer are reported in the United States of America.⁹ Age-adjusted inci-

dence rates are 15.6 per 100,000 for men and 6.1 per 100,000 for women (10.5 for men and women). Higher rates are observed among the black males in USA particularly for oropharynx.

South America and the Caribbean

In South America and the Caribbean, cancers of mouth and pharynx rank fifth in men and sixth in women. The region comprising of Argentina, Southern Brazil and Uruguay has the highest incidence levels, though highest rates are observed in Brazil. Male population in Brazil has the highest risk in the world for cancer of mouth after those in France and India.¹⁰ In 2008, 14,160 new cases of oral and pharyngeal cancer (C00-10) are expected to occur in Brazil (10,380 in males: crude rate 11 per 100,000; 3780 in women: crude rate 3.9 per 100,000).¹¹ It is the 7th most common cancer in the Brazilian population. The distribution of new cases is fairly heterogeneous throughout the states and capital cities of the country, and about 30% of all oral cancers occur in capital cities. In general, Southern and southeastern regions of the country have higher cancer rates while northern and northeastern regions have lower rates (**Figs. 4 and 5**). Of the several population-based cancer registries in Brazil, Sao Paulo and Puerto Alegre have registered highest rates for tongue and mouth cancer.

In the Caribbean, Puerto Rico has the highest reported incidence of oral cancer (>15 per 100,000).¹⁰ In terms of worldwide levels, Cuba has intermediate incidence of cancers of the oral cavity.¹² In males (with a background of heavy cigar smoking) the reported incidence was 7.2 per 100,000 (1986) and has been stable for over a decade.

Africa

Data from Africa are limited to few hospital cancer registries. It is therefore difficult to extrapolate the true incidence in these countries, but reported rates do not show evidence that oral cancer is a serious problem in the African continent. There are descriptive

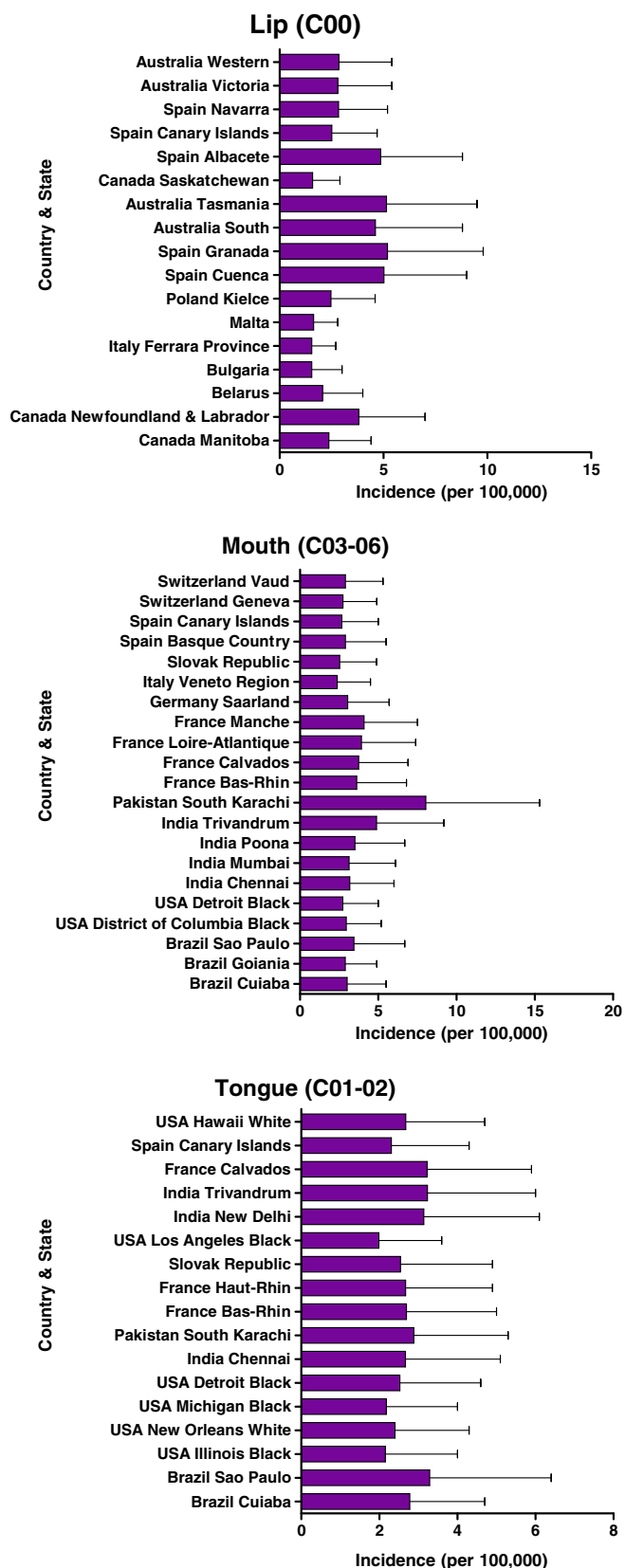


Figure 2. Age-standardised (world) incidence (per 100,000) and standard errors for lip, mouth and tongue cancers in some high incidence countries and regions (extracted from incidence data collected by cancer registries worldwide and published in *C15 (cancer incidence in five continents)*, volume IX, IARC, 2007 – Ref. [2]).

studies from the Sudan that suggest oral cancer rates in males are high, linking this high incidence to toombak, a product of oral snuff mixed with sodium bicarbonate.¹³

Asia

Some countries with the highest incidence rates for oral cancer in the world are located in the region of South Asia. India has always been cited as the country with the highest incidence in the world, though in some recent reports Sri Lanka and Pakistan are ranked at the top. In India alone over 100,000 cases are registered every year. According to *Cancer Incidence in V Continents – vol. VIII*¹⁴ one district of India (Bhopal) has the highest AAR for cancers of both the tongue (10.9 per 100,000) and mouth (9.6 per 100,000) in the world. Ahmedabad urban registry has also a high AAR of 9.3 per 100,000 for tongue cancer. The other urban cancer registries of India have AARs between 3.4 and 6.0.¹⁵ According to Globacan 2002 data¹ Sri Lanka has the highest incidence of oral cancer in the South Asia. It is the most common cancer in males with 15.5% of all cancers reported in the mouth. In the year 2000, age standardised incidence for lip and anterior parts of oral cavity was 10.2 and for posterior mouth and oropharynx was 3.6 per 100,000 (taken together for lip, oral cavity and oropharynx 13.8 per 100,000).¹⁶ More recent records identify South Karachi in Pakistan as having the highest rates² (Fig. 2).

Oral cancer is uncommon in Japan. The incidence rate (C00-14) in Japan in 2001 based on the data from 10 population-based cancer registries was 5.3 per 100,000 adjusted to world population. There were in total 9612 cancers in these sites (6984 in men: 2628 in women).¹⁷

Lip cancer

Highest incidence rates for cancers of the lip are reported in white populations in Canada and Australia (Fig. 2). For example, more than 50% of oral cancers in Australians are located on the lip.¹⁸ It is rare in non-white populations.

Descriptive features associated with incidence data

Migrant studies

Several studies describe patterns of oral cancer incidence among migrant groups, most of which reflect life style influences. Studies on migrants and minority ethnic populations in Britain have reported significantly higher incidence rates in South Asian populations living in Greater London, Birmingham and Yorkshire.^{19,20} Risk of cancer mortality from 1973 to 1985 in persons born in the Indian subcontinent who migrated to England and Wales compared with cancer mortality in the native population, showed substantial highly significant raised risks in Indian ethnic migrants for cancers of the mouth and pharynx.²¹ Other migrant groups that have been studied previously are Indians who migrated to South Africa and to Singapore who have higher rates of oral cancer compared with other nationals in these countries. These findings have challenging implications for sensitive targeting of primary interventions.

Age and sex

In most countries around the world, oral cancer is more common in men than in women. The reported sex differences are attributable to heavier indulgence in risk habits by men and expo-

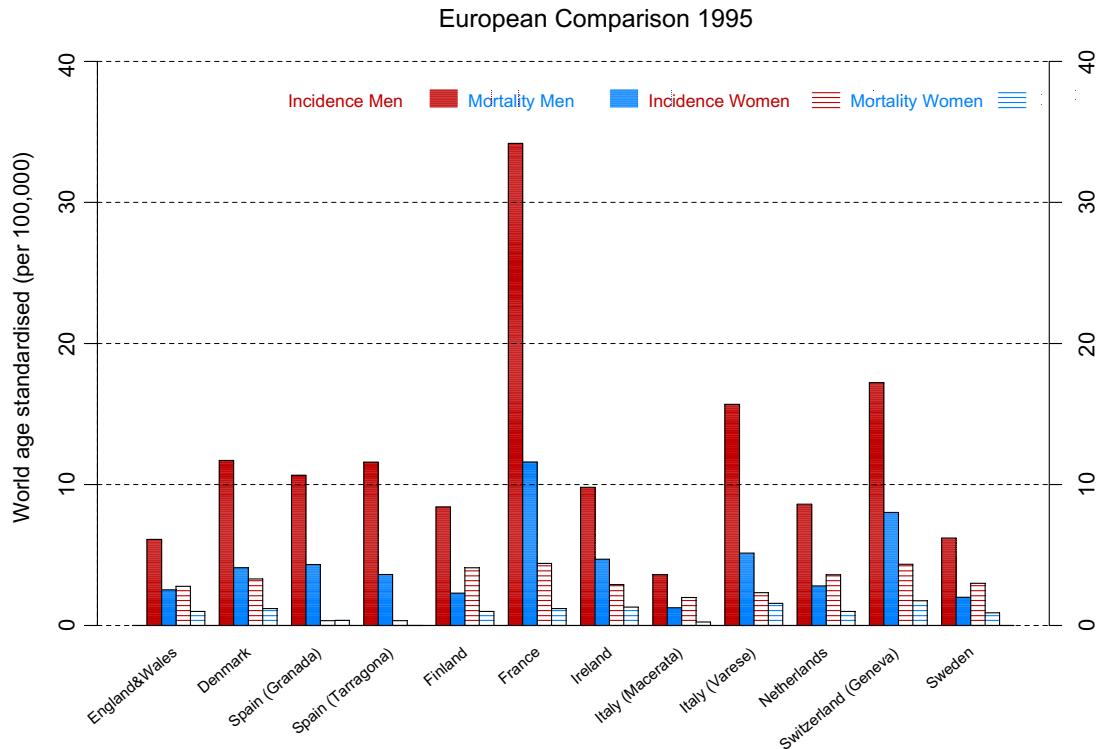


Figure 3. A comparison of incidence of oral cancer among European populations.

sure to sunlight (for lip cancer) as a part of outdoor occupations. The ratio of males to females diagnosed with oral cancer, however, has declined over the decades and is now about 1.5:1 for the mouth and about 2.8:1 for cancer of oropharynx. Thus oral/pharyngeal ratio is lower in men than in women, suggesting that some male characteristic may predispose preferentially to pharyngeal cancer.

The risk of developing oral cancer increases with age and the majority of cases occur in people aged 50 or over. From 2000 to 2004, the median age of diagnosis in USA was 62 years.⁹

Young people

About 6% of oral cancers occur in young people under the age of 45 years.²² In high-incidence countries of the world, many cases are reported before the age of 40.

The rising incidence in oral and oropharyngeal cancer and mortality rates in young adults is reported from many countries in the European Union and parts of United States.^{23–25} In Scotland, where this trend was first reported, the incidence rate between 1990 and 1999 in males under 45 has more than doubled from 0.6 to 1.3 per

Geographic distribution of estimated crude incidence rates per 100,000 men, by State, 2008 (oral cancer).

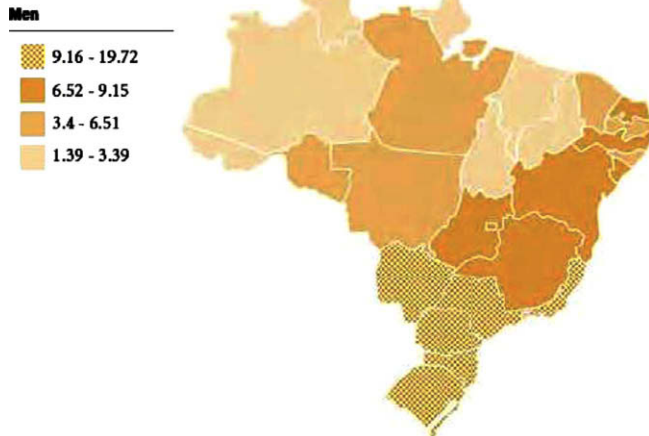


Figure 4. Geographical distribution of oral cancer in Brazilian males.

Geographic distribution of estimated crude incidence rates per 100,000 women, by State, 2008 (oral cancer).

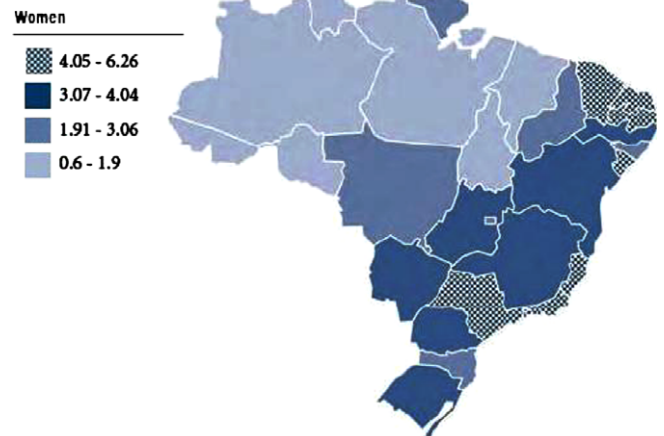


Figure 5. Geographical distribution of oral cancer in Brazilian women.

100,000.⁷ Fortunately the disease is not more aggressive than that occurring in older adults either in the USA or in Southern England.^{25,26}

Anatomic sites

Tongue is the most common site for intraoral cancer among European and the US populations, amounting to 40–50% of oral cancers. Buccal cancer is more common among Asian populations due to betel quid/tobacco chewing habits. In Sri Lanka, 40% of oral cavity cancers are found on buccal mucosa.¹⁶ Other intraoral sites for mouth cancer include floor of mouth, gingivae and palate.

Socio-economic deprivation

Oral cancer is linked to social and economic status and deprivation, with the highest rates occurring in the most disadvantaged sections of the population.²⁷ The association is particularly strong for men. An exception is the young group in which 25% are from professional classes.^{28,29}

Trends

The age standardised incidence of oral cancer in Western Europe has steadily increased in the past two decades. For example in the UK since 1989, an average increase of 2.7% each year has been reported. Increased consumption of alcohol across the UK since post-second World War years has been implicated in the rising trends of oral cancer³⁰; the role of binge drinking remains to be explored.

In the USA, rising trends were noted for incidence in black men from 1974 to 1990. For the period 1995–2004, however, trends for cancer of the oral cavity and pharynx have significantly fallen, with an annual percentage change (APC) of –1.5% for all races (–1.6% for men and –1.8% for women). French data also show a decline for men from 1980 to 2000. The incidence in men fell from 40.2 per 100,000 to 32.2 over 20 years, the annual percentage change from 1978 to 2000 was –1.0%. Incidence in females however, rose from

3.3 per 100,000 in 1980 to 4.7 in 2000. Annual percentage rise was +1.73%. In Japan, the age-adjusted incidence rates doubled from 2.7 per 100,000 in 1975 to 5.4 in 1995, and has stayed stable up to 2001.¹⁷

Survival

Many patients who are successfully treated for oral cancer have to cope with the devastating consequences of their treatment.³¹ These may affect the patient's appearance and function, e.g. eating, drinking, swallowing and speaking. These residual defects may lead to other problems such as depression and nutritional deficiency. Quality of life issues are therefore especially important for this group of patients.

For most countries, five-year survival rates for cancers of the tongue, oral cavity and oropharynx are around 50%. The best outcome is for the cancer of the lip, with over 90% of patients surviving for five years. The lowest survival was for hypopharyngeal tumours. In general, prognosis decreases with advanced disease and increasing inaccessibility of the tumour. For cancers of both the tongue and the oral cavity, women had higher survival rates than men. TNM stage at presentation significantly affects five-year survival. For mobile tongue, five-year survival for stage 1 disease is 80%, while for stage 1V survival drops to 15%.³²

The survival rates for oral cancer in the UK have not shown any improvement over the past three decades. For surviving patients though there is a considerable improvement in the outcome reported in the way their oral and jaw tissues are reconstructed.

As for most oral cancers, survival is better for affluent groups³³ and for younger compared to older patients.^{25,26}

Mortality

For most countries age-adjusted death rates from oral cancer have been estimated at 3–4 per 100,000 men and 1.5–2.0 per 100,000 for women. Mortality from oral cancer had been rising appreciably in most European countries between 1950s and 1980s.³⁴ For example, among the Germans about fourfold in-

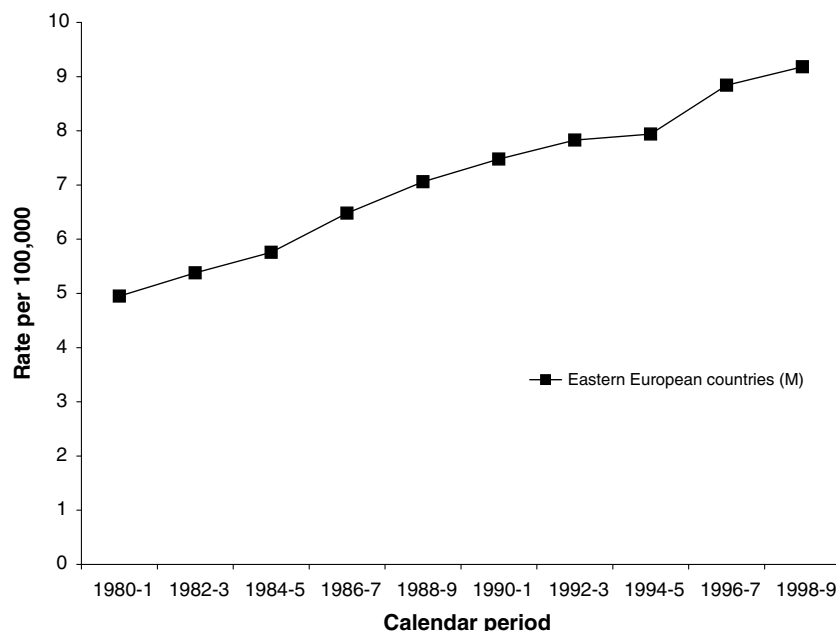


Figure 6. Trends in age-standardised (world population) death certification rates per 100,000 males for oral and pharyngeal cancer in six eastern European countries (Bulgaria, Czech Republic, Hungary, Poland, Romania and Slovakia) 1960–1999 (M = males).

crease was noted during this period. Within the UK mortality rates are highest for Scottish men reflecting their high incidence rates.⁷ Oral cancer mortality among French women has risen in the past 20 years. In 2000, rates stood at 4.7 per 100,000 and annual percentage change of +1.73% was noted between 1980 and 2000.⁵ Most significant rises, as illustrated in Figure 6, were observed in males in six Eastern European countries (Bulgaria, Czech Republic, Hungary, Poland, Romania and Slovakia).³⁴ Exceptional high rates were noted in Hungary in mid-1990s (20.2 per 100,000).

SEER data⁹ for USA report mortality rates of 4.1 per 100,000 men and 1.5 per 100,000 in women based on patients who died in 2000–2004. Mortality rates for black men (6.8) are higher than for other races (white or Hispanic).

Among young people there has been a small but steady increase in mortality rates in most Western countries.²² This is particularly noted for the oropharynx in the US populations.⁹

Second primary tumours

Successful initial treatment with loco-regional control of oral cancer has led to the emergence of second primary tumours (SPT). The relative risk for multiple primary cancer is higher in younger subjects, those who continue to smoke and drink alcohol after therapy, those treated with radiotherapy alone and those treated post-1990 compared with those treated in earlier decades. A study in Southern England has estimated that by 20 years from the time of the first head and neck cancer, approximately 30% of male patients and 20% of female patients will have developed an SPT.³⁵

Risk factors

The etiology of oral cancer is multifactorial. These are discussed in more detail in the paper by Stephano Petti in this supplement. Based on available global evidence the risk factors known to us could be grouped as established, strongly suggestive, possible and speculative factors (see Table 1). The most important etiological factors are tobacco, excess consumption of alcohol³⁶ and betel quid usage³⁷, these factors act separately or synergistically.³⁸ Attributable risk of oral cancer due to both tobacco and alcohol is estimated to be more than 80%. Heavy drinkers and smokers have 38 times the risk of abstainers from both products.³⁸ All forms of tobacco are carcinogenic and evidence for smokeless tobacco causing oral and pharyngeal cancer have recently been evaluated and confirmed.^{39–41} The consumption of fruit and vegetables is found to be associated with a reduced risk of oral cancer, and each portion of fruit or vegetable reduces the risk by at least a quarter.⁴² This suggests a diet deficient in antioxidants is a further factor that predisposes towards the development of oral cancer^{43,44} and for precancer.⁴⁵ Other factors such as HPV infection may also be involved⁴⁶, particularly for tonsil and oropharynx in young people.⁴⁷ Six case-control studies have examined the relationship between tooth loss, periodontal disease and oral cancer, and some have reported significant associations.⁴⁸ Among young people (under the age of 45 years) there is a small sub-group of patients (about 25%) who had little, if any, exposure to the major risk factors.^{28,29}

Table 1
Risk factors for oral cancer and precancer

Established	Strongly suggestive	Possible	Speculative
Smoking	Sunlight (lip)	Viruses	Mouthwashes
Chewing tobacco	Radiation	Immune deficiency	Mate drinking
Snuff dipping		Dentition?	Periodontal disease
Alcohol misuse		Ethnicity?	
Betel quid syphilis			Familial

Only for lip cancers, overexposure to ultraviolet light is implicated.

The presence of potentially malignant oral disorders (mostly caused by similar risk factors, listed in Table 1) could significantly increase the risk of developing mouth cancer.⁴⁹

Delay in diagnosis

Many oral cancers present at a late stage of the disease. Studies examining delay report that patients usually delay seeking professional advice for periods up to 3 months after having become aware of any oral symptom that could be linked to oral cancer. The proportion of patients presenting with advanced disease had not changed in 40 years despite public education.⁵⁰ The responsibility for delay when apportioned to the patient or physician, mostly accounts due to patients' delay. In younger people, this delay could be longer as cancer is not suspected by primary care practitioners.⁵¹

Primary prevention

At least three-quarters of oral cancers could be prevented by the elimination of tobacco smoking and a reduction in alcohol consumption. The removal of these two risk factors also reduces the risk of second tumours in existing oral cancer patients. Smoking cessation contributes to reducing the risk of oral cancers, with a 50% reduction in risk within 5 years.⁵² Ten years after smoking cessation, the risk for ex-smokers approaches that for life-long non-smokers. Treatment of tobacco dependence is an important step to reduce oral cancer in high-risk groups.⁵³ Tobacco cessation among high-risk patients, i.e. those with potentially malignant disorders need to be addressed through the primary care practitioners (including dentists) and where possible with assistance from specialist smoking cessation clinics.^{54,55} Protection against solar irradiation would further reduce the incidence of lip cancers.

In South Asia, efforts are being made to reduce the incidence of the traditional habit of betel quid chewing.⁵⁶ In Thailand where the habit of betel quid chewing has dropped in its popularity, a reduction in the incidence of oral cancer is noted.⁵⁷ Crete and Kaoshung declarations provide a framework for future population activities. Especially in poorer societies, dietary supplementation may help to reduce the risk of oral cancer by chemoprevention targeted at oral premalignant disorders.^{58,59} More research is needed into effective interventions for populations who use betel quid and smokeless tobacco.⁶⁰

Screening (secondary prevention)

Patient delay has been cited as the main reason for late attendance and it seems probable that in both the high-risk and the general population, neither the symptoms of oral cancer nor the main risk factors are well understood.⁶¹ With rising incidence rates, especially in younger age groups whose expectation of cancer is low, public education is urgently needed.⁵¹

It is well established that the treatment of early stage oral cancers achieves higher survival rates with less attendant morbidity and that at present far too many patients present with late stage disease. Therefore, screening for premalignant or early stage oral cancers is worthy of consideration.⁶² Several large population screening programmes from SE Asia and smaller studies from England and Japan were reported during the period 1980–2000.⁶³ However, for low-risk populations, the UK Working Group on Screening for Oral Cancer and Precancer concluded that there was insufficient evidence to support population screening.⁶⁴ Some of the problems include the relative rarity of the disease, a lack of knowledge of the natural history of the disease, disagreement over

disease management and the lack of evidence on the efficacy and cost-effectiveness of different screening methods.^{65,66} One randomized control trial on screening for oral cancer conducted in India has demonstrated a significant mortality reduction in tobacco users.⁶⁷ Opportunistic oral mucosal examinations in dental practices reduces cost of screening and could be an effective model for countries with health care systems that support regular dental attendance.⁶⁸ An alternative strategy would be to conduct screening of high-risk groups⁶⁹, and opportunistic high-risk screening in dental practices may be feasible.⁷⁰ The policy and research for oral screening in different settings are discussed by Warnakulasuriya and Nagao.⁷¹ The educational needs of primary carers including dentists must be addressed and there is still the difficulty of reaching high-risk groups.³¹

Conclusions

Oral cancer remains a lethal disease for over 50% of cases diagnosed annually. This is largely reflected by the fact that most cases are in advanced stages at the time of detection despite easy accessibility of the oral cavity for regular examination. Studies have reported an alarming lack of awareness about oral cancer, its symptoms and causes and these gaps in knowledge need to be addressed by further public education, possibly targeted at high-risk groups.

In order to address delays in diagnosis, the National Institute for Clinical Excellence (NICE) of UK Department of Health took the initiative to set up National Guidelines for referral of suspicious oral lesions to cancer centres. NICE guidelines⁷² on referral pathways should benefit patients. Qualitative studies to understand delays and poor access to treatment centres with the aim of improving the delays of journeys of oral cancer patients would help to improve mortality rates.

With the knowledge of risk factors, primary prevention through the elimination of tobacco consumption, the moderation of alcohol-intake and chemoprevention is urgently needed.

Research on the natural history of the disease, particularly which precancers will progress over time, would help to develop screening programmes tailored more to the individual disorders. Development of tumour markers with high sensitivity and specificity could assist the detection of patients and lesions at risk.

Conflict of Interest Statement

None declared.

Acknowledgements

I wish to gratefully acknowledge several colleagues for permitting to reproduce Figures 3–5. Fig. 3 was supplied by Dr. Laurent Remontet of Service de Biostatistique des Hospices Civils de Lyon Laboratoire de Biostatistique-Santé CNRS/Université Lyon, France, Figures 4 and 5 were supplied by Marceli de Oliveira Santos, Cancer Information Department Prevention Coordination, National Cancer Institute of Brazil – INCA, Brazilian Health Ministry and Figure 6 was kindly supplied by Dr. Fabio Levi, which was modified from an earlier report by La Vecchia et al. (2004) (Ref. [34]).

References

1. Ferlay J, Pisani P, Parkin DM. GLOBOCAN 2002. Cancer incidence, mortality and prevalence worldwide. IARC Cancer Base (2002 estimates). Lyon: IARC Press; 2004.
2. IARC. Cancer incidence in five continents, vol 1X. Available from: <http://www-dep.iarc.fr>.
3. Boyle P, Ferlay J. Cancer incidence and mortality in Europe, 2004. *Ann Oncol* 2005;16:481–8.
4. Black RJ, Bray F, Ferley J, Parkin DM. Cancer incidence and mortality in the European Union: cancer registry data and estimates of national incidence for 1990. *Eur J Cancer* 1997;33:1075–107.
5. Remontet L, Buemi M, Velten M, Jouglà E, Esteve J. Évolution de l'incidence et de la mortalité par cancer en France de 1978 à 2000. Collective expert evaluation report. Lyon: INSERM; 2002.
6. Cancer Research Campaign. CancerStats. Oral cancer – UK. UK: CRC; April 2005.
7. Conway D, Macpherson LMD, Warnakulasuriya KAAS, Ogden G, Stockton DL. Incidence of oral and oropharyngeal cancer in the United Kingdom (1990–1999) – current status, recent trends and intercountry comparisons. *Oral Oncol* 2006;42:586–92.
8. Banoczy J, Squier C. Smoking and disease. *Eur J Dent Educ* 2004;8(Suppl 4):7–10.
9. Surveillance epidemiology and end results (SEER). SEER Cancer statistics review 1975–2004. National Cancer Institute. Available from: <http://seer.cancer.gov/statfacts/html/oralcav> (accessed 03.03.08).
10. Wunsch-Fiho V, de Camargo A. The burden of mouth cancer in Latin America and the Caribbean: epidemiologic issues. *Seminars Oncol* 2001;28:158–68.
11. Brazil: Ministry of Health. Estimate 2008, Brazilian cancer incidence. Rio de Janeiro: National Cancer Institute (INCA); 2007.
12. Garrote LF, Herrero R, Reyes RMO, et al. Risk factors for cancer of the oral cavity and oro-pharynx in Cuba. *Br J Cancer* 2001;85:46–54.
13. Idris AM, Ahmed HM, Mukthar BI, Gander AF, El-Beshir EI. Descriptive epidemiology of oral neoplasms in Sudan 1970–1985 and the role of toombak. *Int J Cancer* 1995;61:155–8.
14. Parkin DM, Whelan SL, Fearlay J, et al, editors. Cancer incidence in five continents, vol VIII. IARC Scientific Publications No. 155. Lyon: IARC Press; 2002.
15. An atlas of cancer in India. Available from: <http://www.cancerindia.org/map.htm>.
16. Ministry of Health. National Cancer Control Programme, Sri Lanka. Cancer incidence data: Sri Lanka year 2000. 6th Publication. Maharagama: NCCP; 2005.
17. Marugame T, Matsuda T, Kamo K, Katanoda K, Ajiki W, Sobue T. Japan cancer surveillance research group. Cancer incidence and incidence rates in Japan in 2001 based on the data from 10 population-based cancer registries. *Japanese J Clin Oncol* 2007;37:884–91. Available from: http://ganjoho.ncc.go.jp/pro/statistics/en/table_download.html.
18. Sugerman PB, Savage NW. Oral cancer in Australia: 1983–1996. *Aust Dent J* 2002;47:45–56.
19. Warnakulasuriya KA, Johnson NW, Linklater KM, Bell J. Cancer of mouth, pharynx and nasopharynx in Asian and Chinese immigrants resident in Thames regions. *Oral Oncol* 1999;35:471–5.
20. Bedi R. Betel quid and tobacco chewing among the United Kingdom's Bangladeshi community. In: The proceedings of the CRC/DoH symposium on cancer and minority ethnic groups. *Br J Cancer* 1996;74(Suppl):S73–7.
21. Swerdlow AJ, Marmot MG, Grulich AE, Head J. Cancer mortality in Indian and British ethnic immigrants from the Indian subcontinent to England and Wales. *Br J Cancer* 1995;72:1312–9.
22. Llewellyn CD, Johnson NW, Warnakulasuriya KAAS. Risk factors for squamous cell carcinoma of the oral cavity in young people – a comprehensive literature review. *Oral Oncol* 2001;37:401–18.
23. Moller H. Changing incidence of cancer of the tongue, oral cavity, and pharynx in Denmark. *J Oral Pathol Med* 1989;18:224–9.
24. Macfarlane GJ, Boyle P, Evstifeeva TV, et al. Rising trends of oral cancer mortality among males worldwide: the return of an old public health problem. *Cancer Causes Control* 1994;5:259–65.
25. Shiboski CH, Schmidt BL, Jordan RC. Tongue and tonsillar carcinoma: increasing trends in the US population ages 20–44 years. *Cancer* 2005;103:1843–9.
26. Warnakulasuriya S, Mak V, Moller H. Oral cancer survival in young people in South East England. *Oral Oncol* 2007;43:982–6.
27. Thames Cancer Registry. Cancer inequalities in London 2000–2004. London: TCR; 2007.
28. Llewellyn CD, Linklater K, Bell J, Johnson NW, Warnakulasuriya S. An analysis of risk factors for oral cancer in young people: a case-control study. *Oral Oncol* 2004;40:304–13.
29. Llewellyn CD, Johnson NW, Warnakulasuriya KAAS. Risk factors for oral cancer in newly diagnosed patients aged 45 years and younger: a case-control study in Southern England. *J Oral Pathol Med* 2004;33:525–32.
30. Hindle I, Downer MC, Moles DR, Speight PM. Is alcohol responsible for more oral cancer? *Oral Oncol* 2000;36:328–33.
31. British Dental Association. BDA occasional paper No. 6. Opportunistic oral cancer screening; April 2000.
32. Rubin PH. Clinical oncology. A multidisciplinary approach to physicians and students. 7th ed. Philadelphia: Saunders; 1993.
33. Edwards DM, Jones J. Incidence of and survival from upper aerodigestive tract cancers in the UK: the influence of deprivation. *Eur J Cancer* 1999;35:968–72.
34. La Vecchia CL, Lucchhini F, Negri E, Levi F. Trends in oral cancer mortality in Europe. *Oral Oncol* 2004;40:433–9.
35. Warnakulasuriya KA, Robinson D, Evans H. Multiple primary tumours following head and neck cancer in southern England during 1961–98. *J Oral Pathol Med* 2003;32:443–9.
36. La Vecchia C, Tavani A, Franceschi S, Levi F, Corrao G, Negri E. Epidemiology and prevention of oral cancer. *Oral Oncol* 1997;33:302–12.
37. International Agency on Research on Cancer. IARC monographs on the evaluation of carcinogenic risks to humans. Betel-quid and areca-nut chewing and some areca-nut related nitrosamines, vol. 85. IARC; 2004.

38. Blot WJ, McLaughlin JK, Winn DM, et al. Smoking and drinking in relation to oral and pharyngeal cancer. *Cancer Res* 1988;**48**:3282–7.
39. International Agency on Research for Cancer. Smokeless tobacco and some tobacco-specific N-nitrosamines. Monographs, vol. 89. Lyon: IARC; 2007. ISBN: 978 92 832 1289 8.
40. Cnattingius S, Galanti R, Grafstrom R, Hergens M-P, Nyren O, Pershagen G, editors. Karolinska institute. Health risks from Swedish snuff; 2005. p. 1–95.
41. Scientific Committees on Emerging and Newly Identified Health Risk (SCENIHR). European Commission; February 2008. Available from: http://ec.europa.eu/health/ph_risk/committees/04_scenih/ docs/scenih_r_o_013.pdf.
42. Warnakulasuriya S. Food, nutrition and oral cancer. In: Wilson M, editor. Food constituents and oral health. Current status and future prospects. Woodhead Publishing; in press.
43. Petridou E, Zavras AI, Lefatzis D. The role of diet and specific micronutrients in the etiology of oral carcinoma. *Cancer* 2002;**94**:2981–8.
44. O'Shaughnessy JA, Kelloff GK, Gordon GB, Dannenberg AJ, Hong WK, Fabin CJ, et al. Treatment and prevention of intraepithelial neoplasia: an important target for accelerated new agent development. *Clin Cancer Res* 2002;**8**:314–46.
45. Nagao T, Ikeda N, Warnakulasuriya S, Fukano H, Yuasa H, Yano M, et al. Serum antioxidant micronutrients and the risk of oral leukoplakia among Japanese. *Oral Oncology* 2000;**36**:466–70.
46. Herrero R, Castellsague X, Pawlita M, et al. Human papillomavirus and oral cancer: the International Agency for Research on Cancer multicenter study. *J Natl Cancer Inst* 2003;**95**:1772–83.
47. D'Souza G, Kreimer AR, Viscidi R, Pawlita M, Fakhry C, Koch WM, et al. Case control study of human papillomavirus and oropharyngeal cancer. *New Eng J Med* 2007;**356**:1944–56.
48. Meyer MS, Josphipura K, Giovannucci E, Michaud D. A review of the relationship between tooth loss, periodontal disease and cancer. *Cancer Causes Control* 2008.
49. Warnakulasuriya S, Johnson NW, van der Wall I. Nomenclature and classification of potentially malignant disorders of the oral mucosa. *J Oral Pathol Med* 2007;**36**:575–80.
50. McGurk M, Chan C, Jones J, O'Reagan EO, Sherriff M. Delay in diagnosis and its effect on outcome in head and neck cancer. *Br J Oral Maxillofac Surg* 2005;**43**:281–4.
51. Llewellyn CD, Johnson NW, Warnakulasuriya S. Factors associated with delay in presentation among younger patients with oral cancer. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2004;**97**:707–13.
52. Samet JM. The health benefits of smoking cessation. *Med Clin North Am* 1992;**76**:399–414.
53. Warnakulasuriya S, Sutherland G, Scully C. Tobacco, oral cancer and treatment of dependence. *Oral Oncol* 2005;**41**:244–60.
54. Poate TWJ, Warnakulasuriya S. Effective management of smoking in an oral dysplasia clinic in London. *Oral Diseases* 2006;**12**:22–6.
55. Ramseer CA, Mattheos N, Needleman I, Watt R, Wickolm S. Consensus report: first European workshop on tobacco prevention and cessation for oral health professionals. *Oral Health Prev Dent* 2006;**4**:7–10.
56. Chiba I. Prevention of betel quid chewers' oral cancer in the Asian Pacific area. *Asian Pacific J Cancer Prev* 2001;**2**:263–9.
57. Reichart P. Oral cancer and precancer related to betel and miang chewing in Thailand: a review. *J Oral Pathol Med* 1995;**24**:241–3.
58. Stich HF, Rosin MP, Hornby, et al. Remission of oral leukoplakia and micronuclei in tobacco/betel quid chewers treated with betacarotene plus vitamin A. *Int J Cancer* 1988;**15**:195–9.
59. Sankaranarayanan R, Mathew B, Varghese, et al. Chemoprevention of oral leukoplakia with vitamin A and beta carotene: an assessment. *Oral Oncol* 1997;**33**:231–6.
60. West R, McNeill A, Raw M. Smokeless tobacco cessation guidelines for health professionals in England. *Br Dent J* 2004;**196**:611–8.
61. Warnakulasuriya KA, Harris CK, Scarrot DM, et al. An alarming lack of public awareness towards oral cancer. *Br Dent J* 1999;**187**:319–22.
62. Napier SS, Speight PM. Natural history of potentially malignant oral lesions and conditions: an overview of the literature. *J Oral Pathol Med* 2008;**37**:1–10.
63. Downer MC, Moles DR, Palmer S, Speight PM. A systematic review of measures of effectiveness in screening for oral cancer and precancer. *Oral Oncol* 2006;**42**:551–60.
64. Speight PM, Downer MC, Zakrzewska J. Screening for oral cancer and precancer. A report of the UK working group on screening for oral cancer and precancer. *Community Dent Health* 1993;**10**(Suppl 1):1–89.
65. Rodrigues VC, Moss SM, Tuomainen H. Oral cancer in the UK: to screen or not to screen. *Oral Oncol* 1998;**34**:454–65.
66. Kujan O, Glenny AM, Duxbury J, et al. Evaluation of screening strategies for improving oral cancer mortality: a Cochrane systematic review. *J Dent Educ* 2005;**69**:255–65.
67. Sankaranarayanan R, Ramadas K, Thomas G, Muwange R, Somanathan T, Mathew B, et al. Effect of screening on oral cancer mortality in Kerala, India: a cluster randomized controlled trial. *Lancet* 2005;**365**:1927–33.
68. Lim K, Moles DR, Downer MC, Speight PM. Opportunistic screening for oral cancer and precancer in general dental practice: results of a demonstration study. *Br Dent J* 2003;**194**:497–502.
69. Harris CK, Warnakulasuriya KAAS, Cooper DJ, Peters TJ, Gelbier S. Prevalence of oral mucosal lesions in alcohol misusers in south London. *J Oral Pathol Med* 2004;**33**:253–9.
70. Speight PM, Palmer S, Moles DR, Downer MC, Smith D, Henriksson M, et al. The cost effectiveness of screening for oral cancer in primary care. *Health Technol Assess Rep* 2006;**10**:1–144.
71. Warnakulasuriya S, Nagao T. Oral cancer and precancer screening: from research to policy and practice. *Global Forum Update Res Health* 2005;**2**:188–91.
72. National Institute for Health and Clinical Excellence (NICE). Improving outcomes in head and neck cancers: the manual. London: NICE; 2004.