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Analysis of oral and pharyngeal cancer rates in Wales

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August 2023

Version 1.0

The report presents the analysis of data from the Welsh Cancer Intelligence and Surveillance Unit relating to cancer of the lip, oral cavity and pharynx.

Oral and oropharyngeal cancers are often referred to as mouth cancer, and include the ICD codes for the lip, oral cavity and oropharynx (C000, C010-C060 and C100). This report provides an update of the 2015 document: Trends in oral and oropharyngeal (mouth) cancer incidence in Wales, 2001-2013 and is an analysis of data from the Welsh Cancer Intelligence and Surveillance Unit. It presents incidence data between 2002 and 2019, mortality data between 2002 and 2021, and survival data up to 2019.

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Key messages

1. More than 300 people in Wales are diagnosed with oral and oropharyngeal (mouth) cancers each year;
2. The main risk factors for these types of cancers are sunlight (lip), tobacco and alcohol (tongue and floor of mouth) and human papilloma virus (oropharyngeal);
3. The incidence rate for mouth cancer has been increasing year on year since 2002 and is twice as common in men than in women;
4. Mouth cancer incidence peaks in seventh decade (60-69 years of age) (Figure 3). Most cases are seen from the age of 40 years of age;
5. The number of men who die from mouth cancer are almost double the number of women (1.94:1);
6. The five-year survival rate for mouth cancer is improving, but remains 50-60% for older age groups.

Key recommendation

Improved survival rates from oral and oropharyngeal (mouth) cancers are dependent on patient recognition and early diagnosis by an appropriate primary care clinician. Further collaboration between Public Health Wales, Health Boards, Primary Care Clusters and the Cancer National Specialist Advisory Group's head and neck clinical group could improve early diagnosis rates in oral and oropharyngeal cancers, and lead to better survival. The Oral Health Foundation have a number of recommendations for mouth cancer, which should be adopted in Wales:

1. Improving education and awareness of the disease to identify mouth cancer and Potentially Malignant Disorders (pre-cancer) (greater support from policymakers, media outlets, celebrities and influencers);
2. Boosting HPV vaccine uptake to reduce the local variations and improve the equity of provision and ensuring all parents of Year 8 and Year 9 children are aware of its importance;
3. Improving access to primary care services for those at risk of mouth cancer and those with mouth cancer;
4. Ensure information and training about mouth cancer continues to form an integral part of Continuing Professional Development (CPD) for dental professionals and ensure mouth cancer information and education should be routinely given to non-dental health professionals;
5. Investing in NHS dentistry to ensure access to services for all; and
6. Reinforcing health policies including strengthening of smoking and alcohol legislation, fiscal measures to further reduce consumption and ensuring all front-line patient-facing clinicians are aware of the risks of mouth cancer and understand how to refer on.

1-Introduction

Oral and oropharyngeal cancers are often referred to as mouth cancer and include the International Classification of Diseases (ICD) coding system codes C00 for the lip, C01-C02 for the tongue, C03-C06 for other parts of the oral cavity and C10 to represent oropharyngeal presentations. The number of people diagnosed with oral and oropharyngeal (mouth) cancers is increasing, with just over 300 people in Wales diagnosed each year from 2013. Although the term commonly describes all lesions in the oral cavity and the oropharynx, there is evidence that this is not a single disease entity and that several variants exist, with different histological and clinical features. The principal difference is that oropharyngeal lesions are associated with infection by human papilloma virus (HPV), while oral cancer is caused by the traditional factors of tobacco and alcohol use.

2-General epidemiology

The *global* incidence of cancers of the lip and oral cavity was estimated to be 377,713 new cases and 177,757 deaths in 2020 (WHO, 2023). However wide variations in trends are reported across the world by sex, age and sub-site (Curado & Hashibe, 2009). Across Europe, the incidence rates of mouth cancer are increasing and unlike the commonest cancers, there has been a substantive increase in new cases (Chaturvedi *et al.*, 2013; CRUK, 2023). The greatest increase in oral cancer has been among younger males in developed countries, where a doubling in incidence has been recorded in men in their 40s and 50s over the last 10 years whilst the mortality rate has remained static owing to the late presentation of the disease (Chaturvedi *et al.*, 2013). Across the United Kingdom, it has been projected that mouth cancer mortality rates will increase by 22.4% by 2030 (CRUK, 2023).

The five-year mortality rate for mouth cancer is improving, but remains at 50-60% for older age groups. In addition, the rate of second primary tumours in these patients is greater than any other type of cancer (3–7% per annum) and is more often the cause of death, compared to any other type of cancer (Day & Blot, 1992; Lippman & Hong, 1989). The most important determinant factor behind these dire statistics is patient and diagnostic delay, as over 60% of patients present with stage III and IV disease (Onizawa *et al.*, 2003; McLeod *et al.*, 2005). Unlike ICD codes C00-C06, there is evidence to suggest that HPV-related oropharyngeal cancer may have a better prognosis (Fakhry *et al.*, 2008). The reasons for this better survival are not clear, but it was also shown that HPV+ lesions are less likely to recur or spread to local cervical lymph nodes although rates of distant metastases were similar (Ang *et al.*, 2010; Fakhry *et al.*, 2014).

The majority of OC are preceded by visible lesions termed Potentially Malignant Disorders (PMDs). This is a state of precancer in the oral cavity that carries an increased risk of progression to squamous cell carcinoma (Napier & Speight, 2008; Warnakulasuriya *et al.*, 2007). The most common PMDs are leukoplakia and erythroplakia meaning white or red plaque respectively. However, variation in the extent of dysplastic change in PMDs means that malignant transformation is difficult to predict (van der Waal, 2009). In a UK practice-based study, 2.7% of cases in a cohort of PMDs underwent malignant transformation (Lim *et al.*, 2003).

3-General aetiology

The highest incidence and mortality rates for oral cancer are seen in the most disadvantaged in the population, where tobacco and alcohol consumption are high (Rogers *et al.*, 2007). In the developed world, tobacco and alcohol use account for the vast majority of leukoplakias. In a dental practice setting in the UK, patients smoking 20 or more cigarettes per day were almost 4 times more likely than non-smokers to have a mucosal lesion (Lim *et al.*, 2003). The type of tobacco usage influences the distribution of the lesions. Equally, regression and/or disappearance of these lesions follows abstinence from tobacco and/or alcohol (Silverman *et al.*, 1984; Marron *et al.*, 2010). Low socioeconomic status is now understood to have an independent effect, beyond its known association with tobacco and alcohol use (Conway *et al.*, 2016; Conway *et al.*, 2008).

The aetiology of lip cancer appears distinct from intra-oral cancer, caused by direct exposure to sunlight (Hindle *et al.*, 2000). In the oropharynx however, HPV infection is found in over 50% of lesions (Stein *et al.*,

2015). The increase in incidence of oropharyngeal cancer appears to be in part due changes in sexual behaviour and to increased carriage of HPV (variants 16/18) in the population. As such, the prevalence of infection and risk of oropharyngeal cancer increases with the number of lifetime or recent vaginal or oral sexual partners (Chattopadhyay *et al.*, 2015; D'Souza *et al.*, 2007).

4-Incidence in Wales

The incidence rate of mouth cancer has increased between 2002 and 2019 (Figure 1). In 2002, the reported number of cases was 171, but this has subsequently increased year on year. From 2013, the number of new cases reported have exceeded 300 per annum and in 2018, this reached its highest incidence of 365.

When comparing men and women, the number of new cases each year for men is nearly double that of women (1.97:1) (Figure 2). Mouth cancer incidence peaks in seventh decade (60-69 years of age) (Figure 3). Most cases are seen from the age of 40 years of age. The most common presentation of mouth cancer is in the tongue, which accounts for 45.2% of all cases (Figure 4). However, the number of oropharyngeal cases is steadily increasing (Figure 5).

Figure 1: Mouth cancer incidence by year (2002-2019)

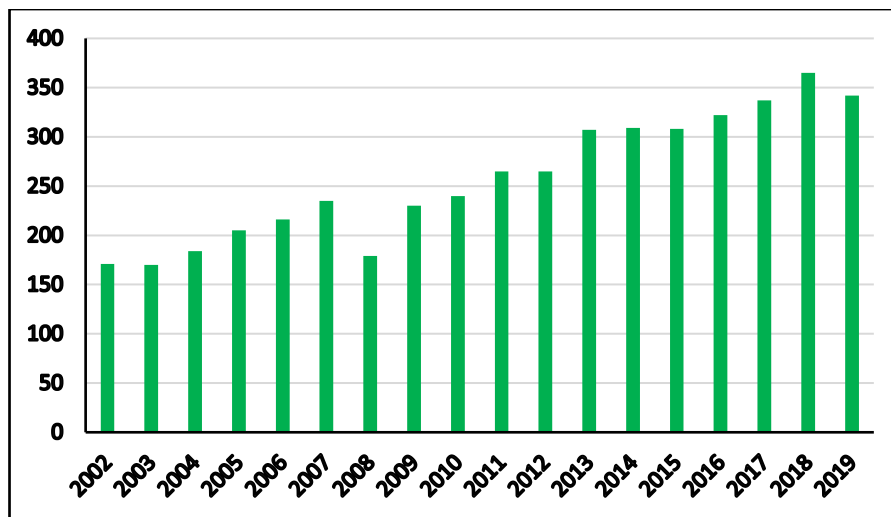


Figure 2: Mouth cancer incidence by sex (2002-2019)

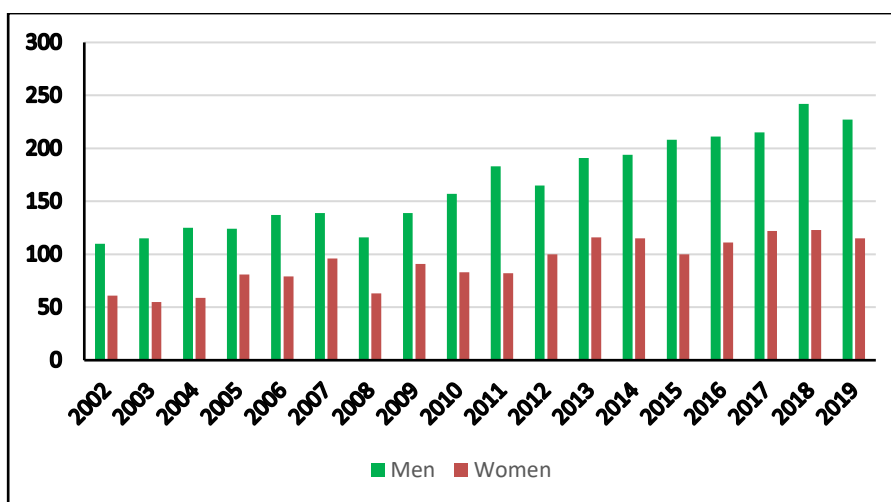


Figure 3: Mouth cancer incidence by age (2002-2019)

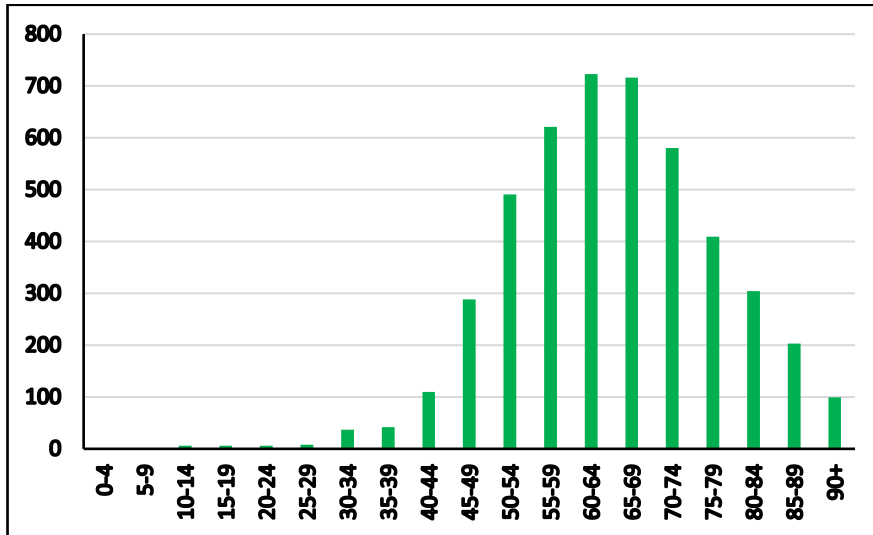


Figure 4: Mouth cancer incidence by cancer type (2002-2019)

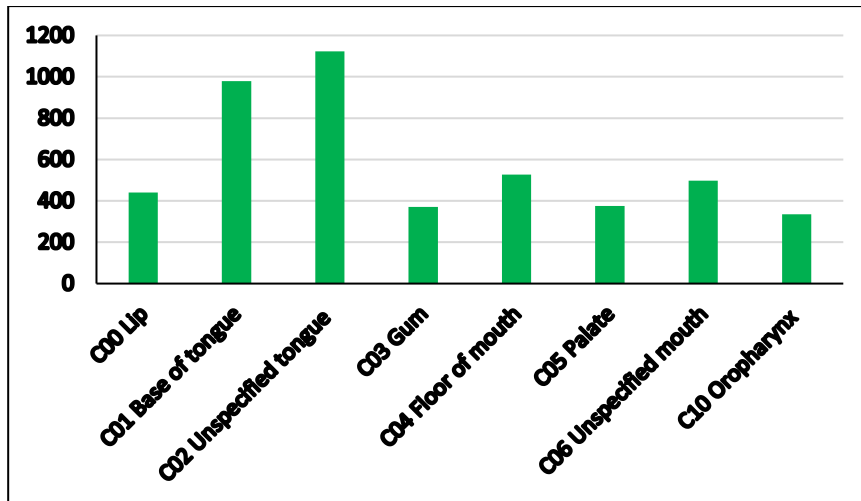
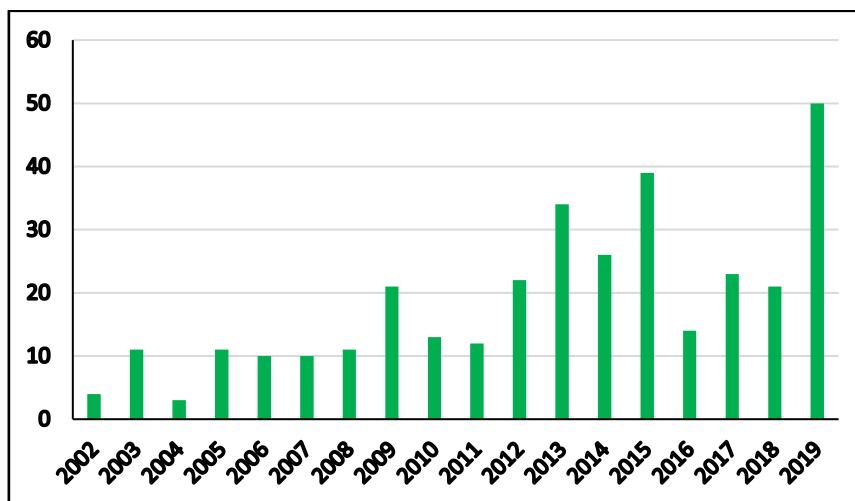


Figure 5: Increase in oropharyngeal cancer incidence by year



5-Mortality and survival

The mortality data from 2002 to 2021 shows a steady increase in the number of deaths from mouth cancer. In 2002, the number of deaths was 57, but by 2021 this had almost doubled to 103 in 2021 (Figure 6). In similarity to the incidence of the disease, the number of men who die from mouth cancer are almost double the number of women (1.94:1) (Figure 7). Mouth cancer mortality again peaks in the first half of the seventh decade (60-64 years of age) (Figure 8). The most common presentation is in the tongue (Figure 9). The survival of men and women with mouth cancer is provided by Figure 10 and 11. It suggests that for both men and women, the survival rate at 5-years is improving slightly, but that there remains a difference between men and women, with slightly poorer survival rates for females. For example, in the 65-74 years age group, survival at 5-years was 50.9% for men and 54.3% for women in 2002, but 60.1% and 50.6% in 2015-19 and 2013-17 respectively.

Figure 6: Mouth cancer mortality by year (2002-2021)

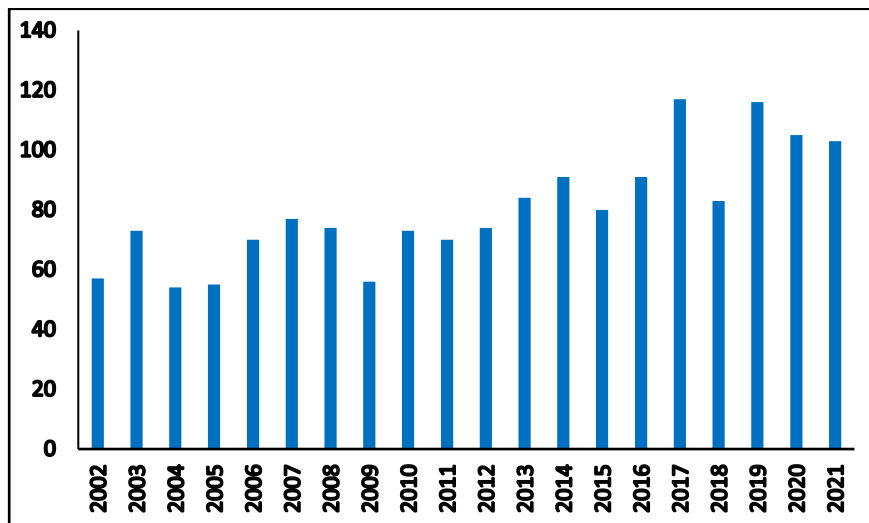


Figure 7: Mouth cancer mortality by sex (2002-21)

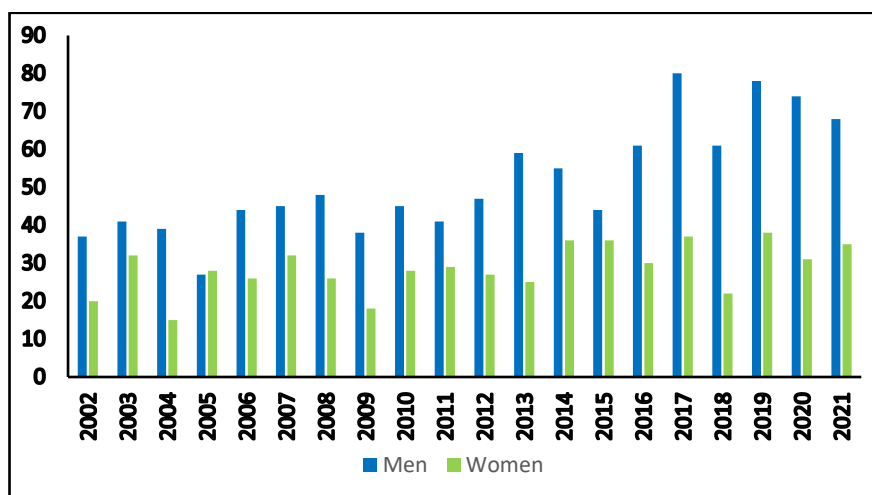


Figure 8: Mouth cancer mortality by age (2002-2021)

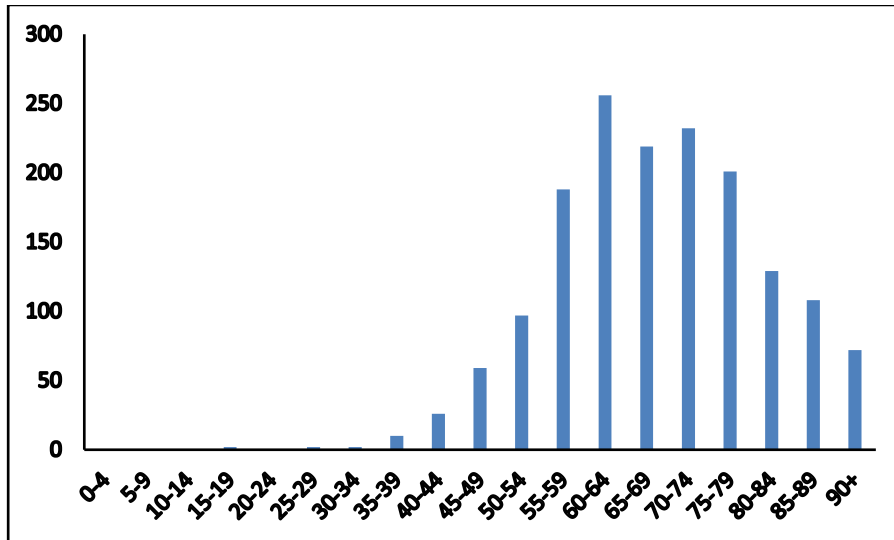


Figure 9: Mouth cancer mortality by site (2002-21)

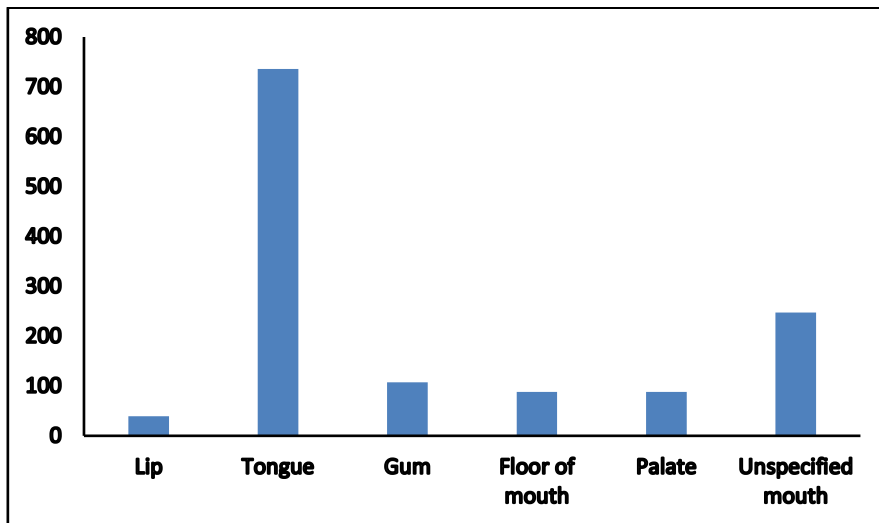


Figure 10: Five-year survival by age group in men (2002-2015)

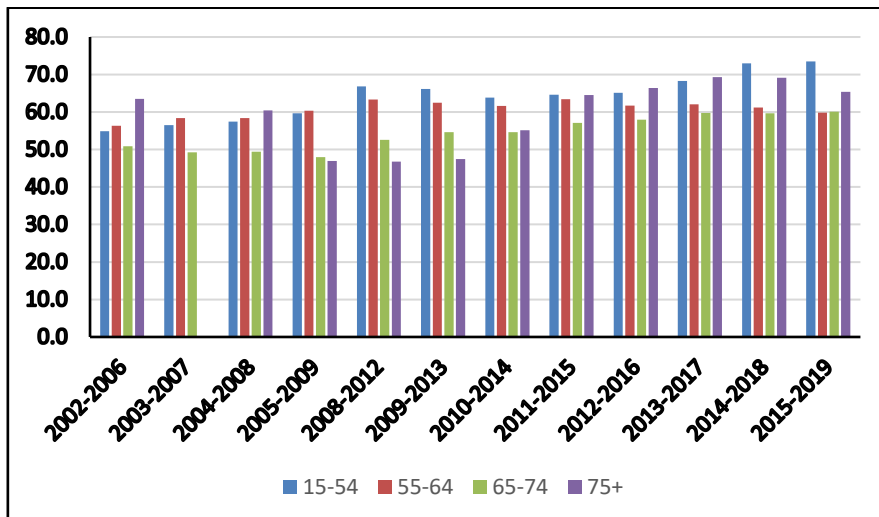
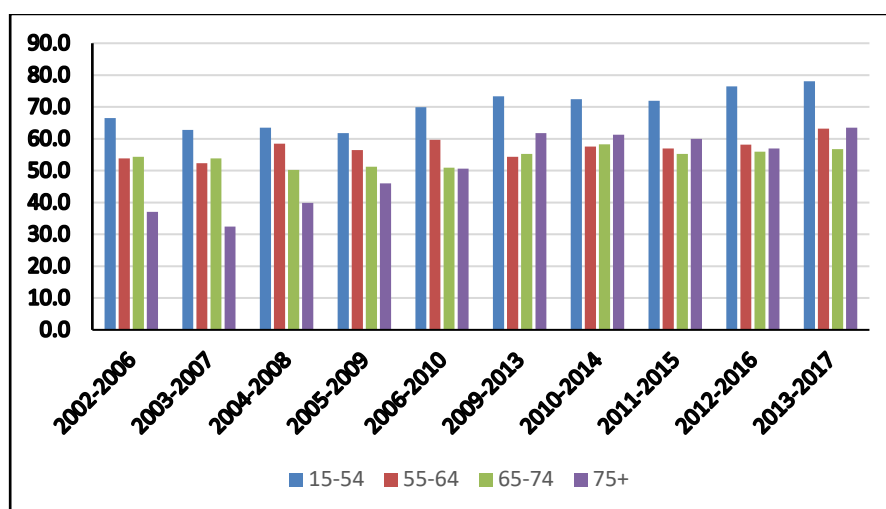


Figure 11: Five-year survival by age group in women (2002-2013)



6- Primary and secondary prevention

The World Health Assembly approved a resolution in 2021 to shift from the traditional curative approach oral health towards a preventive approach (WHO, 2021). Primary and secondary prevention strategies are important in addressing WHO's resolution that oral cancer should be an integral part of national cancer control programmes (Petersen, 2008). Primary prevention aims to prevent a disease from developing, whilst secondary prevention describes a process of early disease detection and preventing the progression of the disease.

Increasing the level of knowledge about oral cancer and its risk factors would appear to be a pre-requisite for facilitating lifestyle changes in mouth cancer. However, up-stream action targeted at educating the population appears to be ineffective, given the low levels of public awareness of the signs, symptoms and risk factors (Scott *et al.*, 2022; Scheideler & Klein, 2018; Peker & Alkurt, 2010; West *et al.*, 2006;). In the United Kingdom, only a third (30%) identify leukoplakia as a possible sign and more than two-in-three (70%) do not know that white patches in the mouth, or a loss of taste, could be a sign of mouth cancer (Scott *et al.*, 2022). However, the use of fiscal measures and legislation to increase the cost of tobacco or ban its use in public places has produced a marked reduction in smoking prevalence and smoking attributable diseases (Levy *et al.*, 2013). Similar approaches have been taken to alcohol in Scotland and Wales and have shown to have a public benefit (Anderson *et al.*, 2021). In the medium term in Scotland and immediate term in Wales, reductions in overall purchases of alcohol appear to impact on those households who purchase the most alcohol.

There is also moderate-quality evidence that some down-stream activities may have some effectiveness, where primary health care workers are used to either educate patients on the harmful effects of known risk factors (tobacco and alcohol use) with targeted behavioural interventions (Kaner *et al.*, 2018; Omaña-Cepeda *et al.*, 2016; Stead *et al.*, 2016). However, these are predicated on attending health services and not all the population has access to a primary provider.

The development of HPV vaccines also shows some promise, particularly quadrivalent vaccines (Gardasil) that act against HPV 16 and 18 and lower risk HPVs (Sinanovic *et al.*, 2009). As such, a number of countries (including the United Kingdom) have expanded vaccination programme to include boys as well as girls, given the decrease in vaccine-type oral or oropharyngeal HPV infections in those immunised with HPV vaccines (Nielsen *et al.*, 2021; Colzani *et al.*, 2021; Schmeler & Sturgis, 2016). Equally, the WHO considers vaccination fundamental for equity in healthcare and beyond. It is one of the key elements of primary healthcare and universal healthcare coverage and the Immunisation Agenda 2030 aims to "extend the benefits of vaccines to

everyone, everywhere” and identifies vaccination ‘coverage and equity’ as one of its seven strategic priorities.

The most researched secondary prevention strategy for mouth cancer is screening, which is defined as “the application of a test to people who are free of the disease in question, in order to identify those who may have the disease and to distinguish them from those who may not” (Wilson & Jungner, 1968). As such, screening is different from case-finding or early detection, which relate to a process of identifying and diagnosing specific lesions either by examination or by an application of a test. Screening describes an on-going process of examination and referral at periodic intervals, applied to a defined population. There are three main types of screening programme: 1) Mass (population) whereby all of the population are screened; 2) Selective where individuals are targeted on the basis of elevated risk and 3) Opportunistic where individuals are examined when they attend a service for an unrelated, purpose. Given that diagnostic delay in mouth cancer is associated with poor prognosis, that the oral cavity is relatively easy to examine and that PMD precedes many mouth cancers, screening could offer a potentially effective public health measure, particularly when undertaken opportunistically (Speight *et al.*, 2016; Brocklehurst *et al.*, 2010; Gomez *et al.*, 2009). There is moderate-quality evidence to support the efficacy of a visual screen for mouth cancer, which forms the basis of most detection methods used (Walsh *et al.*, 2021). Equally, there is evidence of the effectiveness of using a visual screen to reduce the mortality rate and improve the stage shift and survival rates of mouth cancer in population programmes in high-risk areas (Brocklehurst *et al.*, 2013). However, this evidence is limited to one large trial, which had a high risk of bias. Further empirical evidence is required to justify mass or targeted screening programmes in developed countries, given the lower relative incidence and the impact on the cost-effectiveness of the process (Speight *et al.*, 2013).

The Oral Health Foundation have a number of recommendations for mouth cancer:

1. Improving education and awareness of the disease to identify mouth cancer and PMD (greater support from policymakers, media outlets, celebrities and influencers);
2. Boosting HPV vaccine uptake to reduce the local variations and improve the equity of provision and ensuring all parents of Year 8 and Year 9 children are aware of its importance;
3. Improving access to primary care services for those at risk of mouth cancer and those with mouth cancer;
4. Ensure information and training about mouth cancer continues to form an integral part of Continuing Professional Development (CPD) for dental professionals and ensure mouth cancer information and education should be routinely given to non-dental health professionals;
5. Investing in NHS dentistry to ensure access to services for all
6. Reinforcing health policies including strengthening of smoking and alcohol legislation, fiscal measures to further reduce consumption and extending the powers of pharmacists (as a key front-line health worker) to provide referrals.

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