Head and neck cancer risk factors - supplementary information from RCSLT head and neck cancer member guidance

Tobacco

- Smoking is a risk factor for the development of head and neck cancer (Maasland et al, 2014). It negatively affects treatment efficacy and increases likelihood of side effects of treatment or post treatment complications (Bergman et al, 2022) and compromises survival (Lee et al 2022, von Kroge et al 2020).
- Smoking is a greater risk factor individually than alcohol excess, but if combined, alcohol and smoking show a greater than multiplicative risk (Dal Maso et al, 2016, Pezzuto et al, 2015, Mehenna et al, 2010). Smoking combined with alcohol excess is 72%-75% attributable to the risk of developing head and neck cancer, especially laryngeal cancer (Hashibe et al 2009, Hashibe et al, 2007).
- E-cigarettes are implicated in adverse effects on head, neck and oral cells (Wilson et al, 2022) but may help existing smokers quit (Hartmann-Boyce et al, 2016); further research is needed to establish evidence on long term effects. Other methods of tobacco use such as areca nut or betel quid products are linked with high rates of oral cavity cancer in certain populations (Johnson et al, 2020, Zhang et al 2018, Gupta et al, 2018).
- Smoking cessation interventions by healthcare providers can provide positive results (NICE, 2021) if adapted effectively to patients' needs (Khodadadi et al 2021). Smoking cessation counselling can be beneficial with better overall survival for head and neck cancer patients who quit smoking at or around diagnosis compared to continued smokers (Caini et al, 2022).
- Quitting tobacco smoking reduces risks as follows (Shaw and Beasley, 2016, Marron et al, 2010):
  - after 1- 4 years; 35% less risk of developing head and neck cancer
  - after 10 - 15 years; 60% less risk of developing laryngeal cancer
  - after 20 years; down to the risk level of never-smoker for oral cavity cancer
- 60% of smokers stop smoking by 12 months post-diagnosis, but those still smoking at four months after diagnosis are likely to continue (Penfold et al, 2018).

Alcohol

- Alcoholism has been associated with head and neck cancer in 59% of cases in a 12-year analysis of cases (Dhull et al, 2018). Those who drink between 1.5 and six units of alcohol a day increase the risk of mouth cancer by 81% and mouth cancer is 2.5 times higher in regular drinkers than non and occasional drinkers (Oral Health Foundation, 2022).
- Among people who have never used tobacco, high frequency alcohol use (three or more drinks per day) is associated with increased risk of cancers of the oropharynx, hypopharynx and larynx (Hashibe et al, 2008). Alcohol consumption frequency (drinking seven days per

week) increases head and neck cancer (oral cavity, pharynx and larynx sites) risk in moderate to heavy drinkers (Koo et al, 2021).

- Continued alcohol excess post-treatment results in worse quality of life outcomes and a negative impact on survival (especially for laryngeal cancers, Bravi et al, 2021).
- Screening for alcohol dependence and specialist alcohol cessation interventions are effective pre-treatment (Shaw and Beasley, 2016, NICE, 2011). Head and Neck 5000 clinical trial data (Penfold et al, 2018), showed harmful alcohol consumption reduced from 17% at diagnosis to 8% at 12 months, with 21% of people who consumed alcohol above the recommended weekly limit making positive changes. The optimal timing for recommending alcohol and/ or tobacco cessation is during the post-treatment period (Reich et al, 2014).
- After 20 years of quitting alcohol, the risk of head and neck cancer is reduced to the level of never-drinkers (Marron et al, 2010).

Sex

Head and neck cancers are more common in men than women (Conway et al, 2009) with a male to female ratio of 7:1 (Dhull et al, 2018). For male and females who smoke, the risk of developing head and neck cancer is ten and five times higher, respectively, compared to lifetime non-smokers (Dhull et al, 2018).

Age

Incidence rates for head and neck cancer in the UK are highest in people aged 70 to 74 (CRUK, 2021a). Each year, more than a fifth (22%) of all new head and neck cancer cases in the UK are diagnosed in people aged 75 and over (CRUK, 2021a). As we age, our cells and DNA become more damaged either due to the biological process of ageing or from exposure to other risk factors (Oral Health Foundation, 2022).

50% of patients are diagnosed over 60 years of age, but patterns of presentation are changing with younger patients (aged 30-50 years old) tending to present with an isolated neck lump without a history of smoking or heavy alcohol use (Mehenna et al, 2010).

Radiation

This exposure can come from diagnostic x-rays and gamma radiation, or radiotherapy for noncancerous conditions or cancer.

Environmental

Exposure to chemicals such as asbestos, nickel, chromium are risk factors for laryngeal cancer (Hall et al, 2020) and wood dust for nasopharyngeal carcinomas.

Nutrition

Diets high in antioxidant vitamins (especially vitamins C and E) and high in fibre can reduce risk of head and neck cancers (Bravi et al, 2021). Whereas a diet rich in animal fats and cereals is positively associated with laryngeal cancer risk and diets rich in dairy products and breakfast cereals with oral cavity and pharyngeal cancer risk (Bravi et al, 2021). A lack of fruit and vegetables in the diet is associated with 45.4% of laryngeal cancers and 56% of cancers of the lip, mouth and pharynx (PHE, 2016). A diet rich in salted fish is a risk factor for mouth cancer (Oral Health Foundation, 2022) and nasopharyngeal cancer (CRUK, 2021a).

Sunlight

Ultraviolet light and over exposure to sunlight is a risk factor in the aetiology of lip cancer, due to actinic radiation damage (Oral Health Foundation, 2022). Sunbeds increase risk through exposure to UVA and UVB rays and exposure to UV emitting tanning devices is carcinogenic (WHO, 2017).

Infective causes

- Human papillomavirus (HPV, types 16 and 18), is a causative agent for development of oropharyngeal cancer, specifically tumours of the tonsil and base of tongue (Baijens et al, 2021, Shaw and Beasley, 2016). Mehanna et al's (2013) systematic review and meta-analysis found 55% of oropharyngeal cancers were HPV-positive. This rate is increasing; the Oral Health Foundation (2022) report found HPV types 16 and 18 are related to 73% of oropharyngeal cancers and 12% of oral cavity and hypopharynx cancers. HPV-related head and neck cancer has a better survival prognosis compared to head and neck cancer arising from tobacco and alcohol abuse (Wagner et al, 2017). However, tobacco use erases the favourable survival impact of HPV positivity (Elhalawani et al, 2020). Patients presenting with HPV-related oropharyngeal carcinoma tend to be younger (usually 40-50 years old) with a smaller primary and large neck nodes (Mehenna et al, 2010).
- Epstein-Barr virus (EBV) is associated with nasopharyngeal carcinoma (Mehenna et al, 2010).
- Potentially malignant lesions of the mucosa, showing evidence of candida infection have a higher risk of malignant transformation. However, the role of chronic candidiasis in the development of cancer is complex.
- Associations have been found between head and neck cancer and gum disease (for oral cavity cancer only) or poor dental health (measured by number of missing teeth, lack of toothbrushing or less than yearly dentist visit), Hashim et al (2016).

Oncogenes

The role of cancer-promoting genes (oncogenes) and tumour suppressor genes, in relation to head and neck cancer is a complex and rapidly developing field. A family history of head and neck cancer in a first degree relative is associated with a 1.7-fold increased risk of developing the disease (Conway

et al, 2009). Some Gene therapy for 'at risk' individuals and families may hold possibilities for the future.

Pre-existing mucosal abnormalities

Some carcinomas are preceded by premalignant changes. Identification of such changes gives a warning of risk and presents an opportunity for long-term, close follow-up (including biopsy and histopathological assessment) and provision of preventive measures, such as reducing other risk factors.

Premalignant lesions include leukoplakia (associated with oral cavity cancer, Parakh et al, 2020) and erythroplakia. Clinical predictors of malignant transformation include site (high risk in lateral tongue and low risk in floor of mouth), non-homogenous appearance, greater than 200mm in size and higher histological grade (Shaw and Beasley, 2016). Systematic reviews have shown malignant transformation in 12.1 percent of oral dysplasia cases after mean 4.3 years after biopsy (Mehanna, 2009), and 14 percent of laryngeal dysplastic lesions after mean 5.8 years (Weller et al, 2010).

Oral lichen planus is a premalignant lesion in around 1% of individuals. Those with additional epithelial dysplasia are more prone to malignant transformation, particularly in the lateral tongue (Shaw and Beasley, 2016). Proliferative verrucous leukoplakia is a rare condition with 50-80 per cent transformation rates and poor overall prognosis (Shaw and Beasley, 2016).

Social deprivation

Although head and neck cancer occurs in all strata of society, social deprivation is identified as a specific risk. The UK cancer incidence rate increases for laryngeal, lip, mouth and pharynx cancers with increasing levels of deprivation. In England, mouth cancer rates increase by 68% for those living in the most deprived areas (Oral Health Foundation, 2022). Head and neck cancer incidence rates in England in females are 64% higher in the most deprived quintile compared with the least, and in males are 101% higher in the most deprived quintile compared with the least (2013-2017 data, CRUK, 2020). Around 2,300 cases of head and neck cancer each year in England are linked with deprivation (around 520 in females and around 1,800 in males, CRUK, 2020).

Those in the most deprived quintiles are more likely to smoke, drink excess alcohol and less likely to have a diet rich in fruit and vegetables (PHE, 2016). As many as 23% of UK adults have avoided making an appointment at the dentist because of the rise in cost of living and this is a crucial referral route for early diagnosis of head and neck cancer (Oral Health Foundation, 2022). The likelihood of being diagnosed with cancer following an emergency presentation with later stage disease is 50% higher in the most deprived UK population compared to least deprived (Cancer Research, 2020).

The Marmot Review (2020) found smoking is more prevalent among lower socio-economic groups and the differences in smoking prevalence can translate into differences in disease burdens and death

rates between social groups. There is a very strong socioeconomic gradient in survival with lower socioeconomic groups having the lowest survival; sometimes five-year survival is 10-15% higher in the most affluent compared to the most deprived (PHE, 2016).

Social and economic inequalities such as differences in income, education, housing, diet, ethnic group and environment can affect cancer burden, and socially and economically disadvantaged populations have poorer outcomes, later diagnosis, poorer prognosis and inadequate access to treatment, requiring targeted activities to decrease avoidable risk factors (WHO, 2020).

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