Oral cancer risk factors in New Zealand

Muhammed Yakin, Ratu Osea Gavidi, Brian Cox, Alison Rich

ABSTRACT
Oral cancer constitutes the majority of head and neck cancers, which are the fifth most common malignancy worldwide, accounting for an estimated 984,430 cases in 2012. Between 2000 and 2010, there were 1,916 cases of OSCC in New Zealand with a male to female ratio of 1.85:1, and an age-standardised incidence rate of 42 persons per 1,000,000 population.

This article presents an overview of the main risk factors for oral and oropharyngeal cancers and their prevalence in New Zealand. Alcohol consumption is the most prevalent risk factor in New Zealand, followed by tobacco. Given the high prevalence of these two risk factors and their synergistic effect, it is important for doctors and dentists to encourage smoking cessation in smokers and to recommend judicious alcohol intake. Research is needed to determine the prevalence of use of oral preparations of tobacco and water-pipe smoking in New Zealand, especially due to changing demography and increases in migrant populations. UV radiation is also an important risk factor. Further investigations are also needed to determine the prevalence of oral and oropharyngeal cancers attributable to oncogenic HPV infection.

Head and neck cancers are the fifth most common malignancy worldwide, accounting for an estimated 984,430 cases in 2012. Head and neck cancers are cancers arising in the lips, oral cavity, nasal cavity, paranasal sinuses, pharynx, salivary glands and thyroid glands. Approximately half of the head and neck cancers occur in the oral and oropharyngeal regions. There is confusion as to what lesions are classified as ‘oral cancer’, which poses difficulties when comparing different studies. The term oral cancer generally refers to the malignancies of the oral cavity and lip vermilion, 90% of which are oral squamous cell carcinomas (OSCC). In this paper oral cancer will refer to OSCC unless otherwise specified, and thus exclude cancers of the skin of the lips, the oropharynx, all salivary gland and connective tissue neoplasms as well as intra-osseous squamous cell carcinomas.

Between 2000 and 2010, there were 1,916 cases of OSCC in New Zealand, with a male to female ratio of 1.85:1 and an age-standardised incidence rate of 42 persons per 1,000,000 population from 2000 to 2010. The age-specific incidence rates of OSCC steadily increased with age, whereas incidence was highest in the 6th decade of life (Figure 1). The most common site for OSCC was the tongue, which accounted for over 40% of OSCCs, followed by the lip vermilion, which accounted for more than 20% of all OSCCs (Figure 2).

Oral carcinogenesis is a multi-step process that involves progressive genetic mutations affecting tumour suppressor genes and proto-oncogenes, resulting in uncontrolled cell proliferation. Modifiable lifestyle factors such as tobacco and alcohol consumption are considered to contribute in up to 75% of cases of OSCC. Genetic damage from these risk factors tends to accumulate over many years, and hence OSCCs are more common.
in people in their fifth to seventh decades of life than at younger ages.

For intra-oral cancer, the established group of risk factors includes tobacco, alcohol and betel quid chewing, whereas a very small subset are attributable to human papilloma virus (HPV) type 16.8,10,14,15

**Tobacco**

Tobacco use is a key risk factor for the development of oral cancer. Current smokers are at a four-fold increased risk of developing oral cancer compared with non-smokers, and heavy smokers are twenty times more likely to develop oral

**Figure 1:** Average annual age-specific rates and total number of cases of OSCC in New Zealand between 2000 and 2010.

**OSCC in New Zealand, 2000-2010**

<table>
<thead>
<tr>
<th>Age Groups</th>
<th>Number of Cases</th>
<th>Age-Specific Rates</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-9</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>10-19</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>20-29</td>
<td>99</td>
<td></td>
</tr>
<tr>
<td>30-39</td>
<td>220</td>
<td></td>
</tr>
<tr>
<td>40-49</td>
<td>435</td>
<td></td>
</tr>
<tr>
<td>50-59</td>
<td>437</td>
<td></td>
</tr>
<tr>
<td>60-69</td>
<td>410</td>
<td></td>
</tr>
<tr>
<td>70-79</td>
<td>292</td>
<td></td>
</tr>
<tr>
<td>80-89</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Figure 2:** The site distribution of OSCC in New Zealand.

<table>
<thead>
<tr>
<th>Oral sites</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lips</td>
<td>23.8</td>
</tr>
<tr>
<td>Tongue</td>
<td>43</td>
</tr>
<tr>
<td>Gingivae</td>
<td>8</td>
</tr>
<tr>
<td>Floor of Mouth</td>
<td>10.5</td>
</tr>
<tr>
<td>Palate</td>
<td>5.1</td>
</tr>
<tr>
<td>Buccal mucosa</td>
<td>9.6</td>
</tr>
</tbody>
</table>
cancers than non-smokers.\textsuperscript{10} After five years of quitting tobacco smoking, the risk of developing oral and pharyngeal cancers appears to drop substantially.\textsuperscript{10} Tobacco products fall into three main types: rolls, oral preparations and pipes. Rolls include cigarettes, cigars and hand-rolled tobacco products, and are the most common type of tobacco product in New Zealand. The prevalence of the use of pipes and oral preparations in New Zealand is unknown. Most of the available data regarding tobacco smoking in New Zealand refers to the use of cigarettes. There are approximately 4,000 chemicals in cigarettes, many of which are known carcinogens.\textsuperscript{16}

According to the 2015 New Zealand Health Survey, the prevalence of smoking among New Zealand adults decreased from 18% in 2011–2012 to 17% in 2014–2015. In 2014–2015 the percentage of New Zealand adults who smoked daily was 15%. This percentage was highest in adults aged 18–34 years, where approximately one in four adults was a current smoker, whereas only 6% of those younger than 18 years were smokers. Generally, men (18%) were more likely to smoke tobacco than women (15%), but in the Māori population more women (42%) smoked tobacco than men (34%). Smoking rates were higher in more socio-economically disadvantaged areas. The latest data showed that 6% of Asian, 38% of Māori and 25% of Pacific adults were current smokers.\textsuperscript{17}

The New Zealand Ministry of Health provides smoking cessation advice training to all healthcare professionals to support and encourage smokers to quit. A number of nicotine-replacement therapy products are subsidised for this purpose.\textsuperscript{18} It is of utmost importance that doctors and dentists are aware of the prevalence of tobacco smoking among different age groups in their clinic population in order to better provide patients with appropriate smoking cessation advice.

Electronic, or e-cigarettes, are used in some countries to help smokers quit. However, their safety is still a matter for debate. Research has shown that their use, regardless of nicotine content, induces apoptosis and necrosis in epithelial cells. The ability of e-cigarette smoke to induce double-strand DNA breaks and clonal proliferation in oral epithelial cells is also of concern.\textsuperscript{19,20} E-cigarette use among New Zealand youths has tripled since 2012. In 2014, 20% of young people reported having ever used e-cigarettes.\textsuperscript{21} Most adults reported they used e-cigarettes to help them quit, whereas most youths used e-cigarettes because they were curious. There is need for health education regarding the potential risks of e-cigarette use in New Zealand, especially among the young.

Some oral preparations also enhance contact of carcinogens with the oral mucosa. The most common example is betel quid, to which tobacco may also be added. The main ingredient of a betel quid is areca nut wrapped in a betel leaf, usually with slaked lime, with or without the addition of tobacco (Figure 3). The quid is placed in the mandibular buccal sulcus and chewed, producing a mild euphoric effect. Tobacco is an ingredient of the betel quid in some cultures, particularly in India and South East Asia and migrant populations from these regions. The regular use of betel quid, with or without tobacco may lead to the development of sub-mucous fibrosis, a potentially malignant oral disorder.\textsuperscript{9} The use of betel quid without tobacco causes

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**Table 1:** Risk factors for oral cancer grouped according to the level of evidence supporting their carcinogenicity (modified from Warnakulasuriya, 2009\textsuperscript{3} and the IARC\textsuperscript{13}).

<table>
<thead>
<tr>
<th>Established</th>
<th>Strongly suggestive</th>
<th>Possible</th>
<th>Proposed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking</td>
<td>Sunlight (lip)</td>
<td>Human papilloma virus</td>
<td>Mouthwashes</td>
</tr>
<tr>
<td>Chewing tobacco</td>
<td>Radiation</td>
<td>type 18</td>
<td>Mate drinking</td>
</tr>
<tr>
<td>Alcohol consumption</td>
<td></td>
<td>Immune deficiency</td>
<td>Familial</td>
</tr>
<tr>
<td>Betel quid chewing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Human papilloma virus type 16</td>
<td></td>
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a three-fold increase in oral cancer risk in non-smokers and non-drinkers.\textsuperscript{12} When used with tobacco, the risk rises to seven-fold in non-smokers and non-drinkers and to 12- to 22-fold in smokers and drinkers.\textsuperscript{12,22} Very little data is available on the prevalence of use of these oral preparations in people of South East Asian origin now resident in New Zealand.\textsuperscript{23,24} The Oral Pathology Diagnostic Service at the University of Otago has reported eight cases of oral submucous fibrosis from January 2005 to June 2016 from over 23,000 specimen accessions during that period, and all patients were of South-East Asian origin.

Another way to use tobacco products is pipe smoking. This includes direct pipe smoking through a wooden pipe, previously common in Western societies, but now uncommon. This category also includes water-pipe tobacco smoking, also known as shisha, nargileh and hookah. These are particularly popular social outdoor smoking activities in cafes and homes among Middle-Easterners. Water-pipe smoking consists of coals as a heat source often with flavoured tobacco that is smoked through water using pipes (Figure 4). The prevalence of water-pipe smoking in New Zealand is unknown. However, a study carried out in the Arabic-speaking population in south-west Sydney showed that one in four of over 700 participants reported that they smoked water-pipes.\textsuperscript{25} It should be noted that the rate reported in the Sydney study was much higher than that estimated worldwide among Arab youth in the Global Youth Tobacco Survey, where an average of 10.6% of Arab youth reported they were water-pipe smokers.\textsuperscript{26} What is more concerning is the popular belief that water-pipe smoking is less harmful than cigarette smoking. It has been shown that water-pipe use exposes smokers to substantially greater amounts of carcinogens than cigarettes. One 60-minute water-pipe smoking session is estimated to expose the user to carcinogens equivalent to as many as ten cigarettes.\textsuperscript{27} Two other studies have found that water-pipe smokers are at least four times more likely to develop clinically suspicious lesions than non-smokers.\textsuperscript{28,29} Given the lack of data regarding water-pipe smoking in New Zealand, research is required to estimate the actual prevalence of use of water-pipe smoking.

Alcohol

Alcohol is another major risk factor for oral cancer. Regular and heavy alcohol drinkers have approximately two-and-a-half and five times higher risk of developing oral cancer than non-drinkers, respectively.\textsuperscript{10} The effects of alcohol plus tobacco are synergistic. People who are heavy smokers and heavy drinkers are at a 48-fold risk of developing oral and pharyngeal cancers than non-smoking non-drinkers.\textsuperscript{19} In New Zealand, in 2014–2015, 80% of adults drank alcohol regularly.\textsuperscript{17} Among the Asian and Pacific populations of New Zealand, 56% of
adults were regular alcohol drinkers. Of all adult New Zealanders, 18% were defined as hazardous drinkers, that is, had a drinking pattern that caused physical or mental harm to the drinkers themselves or their social circle. People in socioeconomically disadvantaged areas are less likely to be regular alcohol drinkers, but more likely to be hazardous drinkers. The prevalence of hazardous drinking was highest in young adults and in men, where one in four men reported hazardous drinking. A high rate of hazardous drinking was reported among the Māori and Pacific populations; close to one-third and one-fourth of these populations were hazardous drinkers, respectively. The risk of oral and upper aero-digestive tract cancers as a result of alcohol-containing mouthwash use remains controversial. While some studies have found no association, a systematic review has shown that alcohol-containing mouthwash users have a slightly higher risk of oral cancer than non-users.

Ultraviolet radiation

New Zealand has relatively high levels of ambient UV radiation (UV index 13–8 in summer) and relatively low levels of pollution. In addition, approximately 75% of New Zealanders are of European descent with light skin tones and have a liking for the sun. This, coupled with sun protection behaviour patterns, accounts for the high rate of melanoma and non-melanoma skin cancer in New Zealand. While the aetiology of mucosal and skin of lip cancers is different, the lip vermilion is a bridge between the two, and is a common site for oral cancer, as it is directly exposed to UV radiation from sunlight. The magnitude of the risk for developing malignancy depends on the ambient UV radiation, which generally decreases with increasing latitude and duration of exposure determined by lifestyle. In addition, artificial UV radiation such as those used in tanning beds pose a risk of cancer. Although New Zealand has relatively high levels of ambient UV radiation (UV index 13–8 in summer) and relatively low levels of pollution. In addition, approximately 75% of New Zealanders are of European descent with light skin tones and have a liking for the sun. This, coupled with sun protection behaviour patterns, accounts for the high rate of melanoma and non-melanoma skin cancer in New Zealand. While the aetiology of mucosal and skin of lip cancers is different, the lip vermilion is a bridge between the two, and is a common site for oral cancer, as it is directly exposed to UV radiation from sunlight. The magnitude of the risk for developing malignancy depends on the ambient UV radiation, which generally decreases with increasing latitude and duration of exposure determined by lifestyle. In addition, artificial UV radiation such as those used in tanning beds pose a risk of cancer.
Zealanders do not have a higher lip to oral cavity SCC ratio than other populations, protection from UV radiation is essential to avoid lip and skin cancers.

**Human papilloma virus**

High risk, or oncogenic, HPV types are those that integrate their genome into the host DNA and subsequently produce E6 and E7 oncogenes, which work to deregulate key molecules involved in the cell cycle.\(^{36,37}\) The aetiopathogenetic role of HPV in head and neck cancers, specifically oropharyngeal carcinoma and tonsillar carcinoma, has been established. People who develop these cancers have distinct demographic features, as they particularly affect younger individuals in their third or fourth decades of life.\(^{11,13}\) The role of HPV infection in the pathogenesis of OSCC is less certain.\(^{15,38}\) The rate of HPV-positive OSCC has been estimated to be 1–3%, which is much lower than that of oropharyngeal SCC, in which HPV-positive SCCs contribute as much as 65%.\(^{14,15,38}\) There are a number of methods used to detect the presence of HPV in tissues. The tumour suppressor protein p16 serves as a useful surrogate marker for significant infection by high-risk HPV and its E7 oncogene,\(^{39}\) and can be detected on formalin-fixed specimens using immunohistochemistry (IHC). However, p16 IHC alone is insufficient to confirm the involvement of high-risk HPV.\(^{40}\) Detection of viral oncogenes using polymerase chain reaction (PCR) of E6/E7 mRNA, quantitative PCR, or in-situ hybridisation of viral DNA or mRNA are required to confirm the role of HPV in carcinogenesis. This information is important, at least for some head and neck squamous cell carcinomas (HNSCC), since high-risk HPV-positive HNSCC, including oropharyngeal carcinoma, is more responsive to radiotherapy, and has a better prognosis than conventional SCC.\(^{41-43}\) It is not yet clear whether HPV status influences the prognosis of OSCC.

HPV vaccination programmes for young females have been in place in New Zealand since 2008, as well as in Australia where the programme includes both males and females.\(^{44,45}\) The vaccination programme is to be extended to boys in New Zealand. One study reported the presence of high-risk HPV in the oral cavity of two of 219 New Zealand women.\(^{46}\) Another study showed that 41 of 55 patients investigated had HPV-related oropharyngeal cancers.\(^{47}\) No other data exists regarding the presence of high-risk HPV in the oral and oropharyngeal sites of New Zealanders.

**Conclusions**

This paper presented an overview of the main risk factors for oral and oropharyngeal cancers and their prevalence New Zealand. Alcohol consumption is the most prevalent risk factor in New Zealand, followed by tobacco. Given the high prevalence of these two risk factors and their synergistic effect, it is important for doctors and dentists to encourage smoking cessation in smokers and to recommend judicious alcohol intake. Research is needed to determine the prevalence of use of oral preparations of tobacco and water-pipe smoking in New Zealand, especially due to changing demography and increases in migrant populations. UV radiation is also an important risk factor. Further investigations are also needed to determine the prevalence of oral and oropharyngeal cancers attributable to oncogenic HPV infection.
Competing interests:
Nil.

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REFERENCES:


