

# Oral cancer – the fight must go on against all odds...

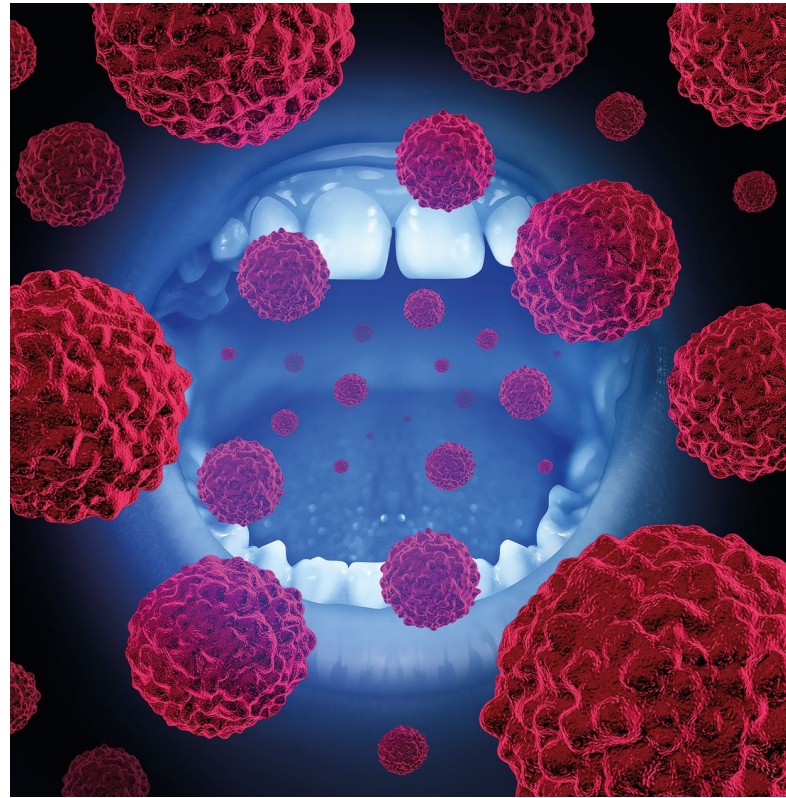
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Oral squamous cell carcinoma (OSCC) arising from the oral cavity and lips constitutes one of the most common types of malignancy in the head and neck region. Data from the Global Cancer Observatory (GCO) shows that the annual incidence of OSCC in 2020 was 377,713 cases worldwide, with the highest number recorded in Asia (248,360), followed by Europe (65,279) and North America (27,469).<sup>1</sup> The five-year prevalence of OSCC approached nearly one million (959,248) and followed the same pattern; that is, highest in Asia, followed by Europe and North America. These figures do not include squamous cell carcinoma arising from the mucosal epithelium in the oropharynx, oesophagus, nasopharynx, or larynx. It is also worth mentioning that the incidence and prevalence of OSCC may be underreported from less developed countries due to inadequate documentation of data. Nevertheless, the available data on OSCC highlights that it is a major health concern and is associated with high rates of mortality and morbidity. Despite numerous improvements in cancer management, only modest improvements have been achieved in the survival rates of head and neck cancers.<sup>2</sup> Unfortunately, there is no end in sight for the foreseeable future and the burden of OSCC is expected to rise. According to the GCO, by 2040, the incidence of OSCC is predicted to increase by up to 40% with a corresponding increase in mortality.

Smoking and alcohol consumption are two of the most recognised risk factors for oral cancer and work synergistically to increase the risk by up to 35%.<sup>3</sup> As per World Health Organisation figures, tobacco is responsible for over eight million deaths annually, and there are approximately 1.3 billion tobacco users worldwide and over 80% of these are based in low- and middle-income countries. Similarly, alcohol consumption is responsible for up to three million deaths annually. While the public health campaigns against smoking have led to reductions in the number of smokers in developed countries, the message against

alcohol use has been relatively mild. There is growing evidence that no amount of alcohol is safe and healthcare providers need to revisit the existing guidance on 'recommended' limits of alcohol.<sup>4</sup> The message needs to be loud and clear that zero alcohol consumption is the best way to minimise health loss.<sup>5</sup> Areca nut consumption also has a strong association with OSCC and is mainly observed in East Asian and Pacific populations. Again, targeted awareness and public education coupled with government regulation to minimise areca nut consumption is the way forward.

Electronic cigarettes and vaping devices have been marketed aggressively over the last decade as a 'safe' alternative to cigarettes without any long-term data to support these claims. Unfortunately, healthcare providers have been less cautious in their recommendations regarding use of electronic cigarettes for smoking cessation. There is a growing body of reports regarding harmful effects of electronic cigarettes on cardiovascular and pulmonary health, apart from numerous other health risks. A variety of definite and probable carcinogens have been identified in electronic cigarette liquids including nicotine derivatives, polycyclic aromatic hydrocarbons, heavy metals, aldehydes etc.<sup>6</sup> Extrapolation of data from smokers indicates lag times of approximately 20–25 years before development of cancer and therefore the carcinogenic potential of electronic cigarettes needs more time to be fully established. A general consensus



appears to be emerging that electronic cigarettes should be subjected to the same regulatory policies as traditional cigarettes.

Infections with human papillomavirus (HPV) and Epstein-Barr virus (EBV) are also recognised risk factors for cancers involving the mouth and upper aero-digestive tract. Given the availability of HPV vaccines, it is possible to prevent HPV-associated cancers. While HPV vaccinations are being implemented in developed countries, more efforts are required to make these available globally. Moreover, dental professionals need additional training to provide effective patient education on the cancer risks of HPV infection which is often related to oral sexual practices and requires sensitive communication.<sup>7</sup>

As with many other types of cancers, a significant proportion of OSCCs are detected at a late stage, leading to poor survival rates and high morbidity despite costly investigations and treatments.<sup>8,9</sup> Mass screening for OSCC poses several challenges, and cost-effectiveness is a major barrier in

implementation of formal national oral cancer screening programmes.<sup>10</sup> Moreover, access to dental care is not always available, especially in many less developed countries, which further reduces the chances of opportunistic oral cancer screening during clinical examinations by dental professionals.<sup>11</sup>

Nevertheless, it is not total doom and gloom in our fight against oral cancer. Improved access to epidemiological data, advances in molecular biology, genetics, diagnostics and treatment modalities will eventually translate into improvements in cancer prevention and care. Rapid developments in the field of artificial intelligence (AI) offer a glimmer of hope for mass oral cancer screening.<sup>12</sup> AI tools with high sensitivity and specificity for oral cancer screening are currently being investigated and, potentially, AI-based mobile applications could be used not only by frontline healthcare workers but also by the public. Such technological advances may enable early recognition of suspicious lesions and facilitate early referral and management. Recent advances in immunotherapy – such as the use of immune checkpoint inhibitors (ICIs), especially programmed death-1 (PD-1)/programmed death-ligand 1 (PD-L1) inhibitors – also show immense promise for the management of OSCC. PD-1 is a checkpoint protein on T lymphocytes which prevents T cells from attacking cancer cells. Multiple clinical trials provide evidence to support the use of PD-1 inhibitors to prolong survival in recurrent

and metastatic squamous cell carcinoma of the head and neck.<sup>13</sup> Anti-PD1 monoclonal antibodies nivolumab and pembrolizumab boost the immune response against cancer by enhancing recognition and destruction of cancer cells by T cells. These drugs have been shown to be superior to aggressive combination chemotherapy.

Internet connectivity and availability of social media platforms offer immense potential for raising public awareness and mass education regarding risk factors for OSCC on a global scale. Resources aimed at sensitising the public to risk factors for oral cancer can be produced in multiple languages for the benefit of populations in various geographic locations at a significantly lower cost. Learning from breast cancer awareness campaigns, active involvement of oral cancer patients in public awareness campaigns are likely to be more impactful in comparison to education by professionals alone.<sup>14</sup> Notwithstanding the challenges in the prevention and management of OSCC, exceptional commitment and dedication of multidisciplinary head and neck cancer teams working relentlessly across the globe needs to be acknowledged. Clinicians, scientists, allied healthcare workers and policymakers must continue their excellent work against all odds and the fight against oral cancer must go on...

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## Correction to: Volume 22 Issue 4, December 2021

The issue can be found online at <https://www.nature.com/ebd/volumes/22/issues/4>

Journal's correction note:

Summary Review *Evid Based Dent* 2021; <https://doi.org/10.1038/s41432-021-0214-y>  
 Summary Review *Evid Based Dent* 2021; <https://doi.org/10.1038/s41432-021-0215-x>  
 Summary Review *Evid Based Dent* 2021; <https://doi.org/10.1038/s41432-021-0226-7>  
 Summary Review *Evid Based Dent* 2021; <https://doi.org/10.1038/s41432-021-0227-6>  
 Summary Review *Evid Based Dent* 2021; <https://doi.org/10.1038/s41432-021-0218-7>  
 Summary Review *Evid Based Dent* 2021; <https://doi.org/10.1038/s41432-021-0219-6>  
 Summary Review *Evid Based Dent* 2021; <https://doi.org/10.1038/s41432-021-0228-5>  
 Summary Review *Evid Based Dent* 2021; <https://doi.org/10.1038/s41432-021-0220-0>  
 Summary Review *Evid Based Dent* 2021; <https://doi.org/10.1038/s41432-021-0213-z>  
 Summary Review *Evid Based Dent* 2021; <https://doi.org/10.1038/s41432-021-0216-9>  
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Due to a production error, when Volume 22 Issue 4 of *Evidence-Based Dentistry* was originally published, the publication date on the publisher's internal portal read 16 December 2021. This has been corrected to 17 December 2021.

In addition, when originally published, four systematic reviews which were included in this issue were omitted from the online issue Table of Contents. These four systematic reviews have now been added accordingly.

The journal apologises for any inconvenience caused.