



Scoping review of the opportunities to escape oral cancer

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Abstract

Background: With a high rate of death and morbidity, oral cancer ranks as the sixteenth most prevalent cancer worldwide. According to the Global Cancer Observatory (GLOBOCAN) of the International Agency for Research on Cancer (IARC), there were 177,757 oral cancer-related deaths and 377,713 new cases globally in 2020. Oral cancer in India comprises 45% of the global disease burden. Men (incidence rate: 13.1 per 100,000) are 2.62 times more likely to be affected by head and neck cancer than women (5 per 100,000) and experience double the corresponding mortality rates. The high prevalence, incidence, and excruciating nature of the disease necessitated this review to outline potential precautions and prophylactic interventions to be undertaken to prevent this agonizing and highly fatal disease in order to sensitize healthcare workers and train them to fight this disease.

Methods: The search analysis from PubMed, the World Health Organisation (WHO) International Clinical Trials Registry, Cochrane Reviews, and CENTRAL yielded a list of comprehensive strategies used in different geographic locations to prevent this deleterious health issue.

Results: The results include evidence of interventions that have successfully prevented oral cancer in different sections of the population. In addition to controlling tobacco use and herpes virus infection, these interventions include community health programs, primary healthcare workers and dentists, chemopreventive agents, herbal extracts, and artificial intelligence models.

Conclusion: Oral health is one factor affecting well-being, so a preventive approach must be considered to ensure its achievement.

Keywords: Oral health, Prevention of oral cancer, Oral malignancy, Oral squamous cell carcinoma

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Introduction

Oral cancer is the sixteenth most common cancer type globally, and it is the cause of significant rates of mortality and morbidity. According to the GLOBOCAN of the IARC, there were 177,757 oral cancer-related deaths and 377,713 new cases globally in 2020.¹ Oral cancer in India comprises 45% of the global disease burden. Men (incidence rate: 13.1 per 100,000) are 2.62 times more likely to be affected by head and neck cancer than women (5 per 100,000) and experience double the corresponding mortality rates. As treatments may be linked to significant oral difficulties, the adage “Prevention is better than cure” can also be applied to the prevention of oral cancer. Because most people have access to mobile phone networks, reports of oral cancer screening and early detection utilizing mobile health (mHealth) technologies are available.²

Oral disorders account for most non-communicable diseases, and they affect over half of the world’s population, which means that they affect approximately 3.5 billion individuals worldwide, ranging from infants to adults. The world health organization’s Global Oral Health Status Report (GOHSR) presents the first all-inclusive analysis of the burden of oral diseases. It identifies obstacles and

chances to facilitate the transition to universal oral health coverage. Fundamentally, prevention involves eliminating risk factor vulnerabilities and educating the public about these risks, including tobacco and alcohol use and their associated side effects.³ It also involves teaching the medical professional⁴ how to counsel patients regarding risk factors associated with oral cancer.⁴⁻⁷ Advanced preventive techniques can be utilized to identify, diagnose, and treat premalignant lesions as soon as possible. Artificial intelligence can also prevent malignancies in the head and neck region.⁸

Materials and Methods

Background

The use of tobacco and alcohol products increases the risk of oral cancer, which is widespread among men in developing and underdeveloped nations. There can be many more preventive strategies. Some are detailed here and confirmed by some randomized control trials and other types of health research.

Objectives

To identify evidence-based preventive strategies for oral



cancer from different locations.

To assess the effectiveness, safety, and acceptability of such preventive strategies.

Search Methods

The world health organization's International Clinical Trials Registry Platform (clinicaltrials.gov) (from 2000 until 11 January 2024), PubMed (from 2000 until January 2024), Cochrane Reviews (from 2000 to date), and CENTRAL (from 2000 to date) are four electronic databases that were searched in this review. Google Scholar was skimmed through visually to identify any missing articles. When scanning electronic databases, articles in the English language were given preference.

Selection Criteria

MeSH words were included to maximize sensitivity. EndNote was used to manage the references and remove any duplicates. The words "oral malignancies of teeth/oral cavities" were identified. For simplicity, all cancers of the lip and oral cavity listed in the world health organization (WHO) report were referred to as "oral cancer/oral carcinoma." Open-source databases such as Cochrane Library, PubMed, and some grey Literature were used, as listed in Table 1. Table 1 takes the form of a population, intervention, comparison, and outcome of interest (PICO) chart which helps in structuring the clinical question and inclusion/exclusion criteria for research studies. It also defines which participants are suitable for the study, what interventions will be tested, and what outcomes will be measured, ensuring clarity and focus in the research design.

Inclusion Criteria

Studies on patients diagnosed with oral cancer, encompassing various stages, types, and demographic groups, interventions covering a broad spectrum, including surgical, radiation, chemotherapy, immunotherapy, and combination treatments, as well as diagnostic methods, prevention, and screening strategies, comparisons between different interventions, treated and untreated groups, and novel therapies versus standard care, and a range of research methodologies, including qualitative investigations, case-control studies, cohort

studies, systematic reviews, cross-sectional studies, and meta-analyses were covered. Studies published in English from the year 2000 were prioritized to maintain a focus on current knowledge.

Exclusion Criteria

Studies focusing on cancers other than oral cancer or solely on precancerous lesions were excluded. Research that did not evaluate specific interventions or treatments for oral cancer, particularly those without direct clinical application, was omitted. Studies lacking a clear comparison group or comparative analysis and those without relevant clinical or patient-reported outcomes were not included. Case reports, series with small sample sizes, opinion pieces, editorials, and non-peer-reviewed articles were also excluded. To maintain a focus on current and relevant research, studies published in languages other than English, except for seminal works and those published more than 25 years ago, were generally excluded.

Results

This review article is based primarily on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR). The flow diagram depicted in Figure 1, illustrates the literature search results in this scoping review. PRISMA-ScR provides a structured framework for reporting scoping reviews, ensuring they are transparent, reproducible, and thorough. It includes a checklist of 20 essential and two optional items covering various review aspects: title, abstract, rationale, objectives, eligibility criteria, information sources, search strategy, selection process, data charting, data items, critical appraisal, synthesis of results, summary, conclusions, funding, data availability, registration, protocol, introduction, methods, results, and discussion. Adhering to these guidelines has helped produce methodologically sound scoping reviews that offer valuable insights and communicate their findings and implications, which are as below.

A total of 127 articles were obtained, including three from the WHO Clinical Trials Registry, one from Cochrane Reviews, 7 from CENTRAL, and 124 from PubMed. After duplicate elimination, 66 records were considered potentially eligible, and finally, 24 studies were evaluated

Table 1. PICO(S) chart for studying oral cancer prevention

PICOS – Forming the research question	Inclusion criteria	Exclusion criteria
Population	<ul style="list-style-type: none"> Adults above 18 years High-risk groups People with precancerous lesions 	<ul style="list-style-type: none"> Individuals below 18 years Individuals with severe comorbidities or current diagnosis of oral cancer
Intervention	Preventive measures	n-preventive measures like treatment of existing illness
Comparator	Comparison with the control group	Not applicable
Outcome	<ul style="list-style-type: none"> Early detection Reducing incidence 	<ul style="list-style-type: none"> Unrelated outcomes like dental hygiene Lack of follow-up
Study Design	All types	Not applicable

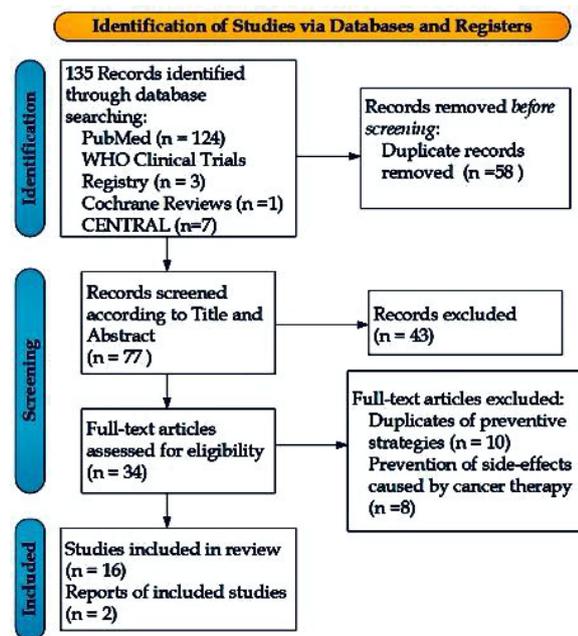


Figure 1. Data analysis - PRISMA-ScR for prevention of oral cancer

in their full text, and 18 studies were evaluated for further evidence synthesis and critical analysis. Table 2 was produced as a data abstraction sheet for review and further discussion.

Discussion

mHealth / Mobile Health Technology of WHO

Most people have access to a mobile phone network. Reports of oral cancer screening and early detection utilizing mobile health (mHealth) technologies are available. Some studies have documented the innovations in mobile applications and mHealth devices, along with the viability of some mHealth initiatives for the early diagnosis of oral carcinomas. Community health workers might recognize “abnormal” oral lesions by accessing an app on their phone.² Remote diagnosis of malignancies in the head and neck region for early detection is feasible and beneficial, especially in remote settings.¹¹

Role of General Practitioners in Accelerating Prevention

The low survival rates of oral cancer may be improved by programs that encourage early diagnosis in general practice, such as opportunistic screening of high-risk patients. There is evidence that timely diagnosis and effective treatment can prolong life. In order to better understand the symptoms of oral cancer and the role general practitioners play in patient identification and referral, 200 patients participated in a UK study in which they were sent questionnaires describing their symptoms, GP consultation outcomes, and diagnoses. Of the 161 individuals, 32% and 56% had been referred to secondary treatment by their dentist and general practitioner, respectively. Mouth ulcers and tumors in the face or neck

were the most often reported symptoms (32%).¹¹ This targeted approach is suggested to increase care among the population vulnerable to head and neck cancers.⁴

Effectiveness of Screening Programmes

It has been demonstrated that oral cancer screening can save a life in only five minutes.^{9, 23} According to Sankaranarayanan et al, visual inspection and screening can reduce at least 37,000 oral cancer deaths globally by lowering mortality in high-risk patients.¹⁰ Figure 2 is a summative figure of one such preventive screening camp, conducted in a primary school in Chennai, which is in the south of India.

Significant Contribution by Primary Healthcare Workers and Auxiliaries

Oral malignancies are estimated to account for 35–40% of all cancer cases; they can be cured if diagnosed early. In a field study conducted in Sri Lanka, the hypothesis was that using primary healthcare providers could be a feasible way to identify oral cancer in developing nations at an early stage. Subjects with oral lesions were identified by medical and dental officials in a control region. Over 52 weeks, 34 primary healthcare providers examined the oral cavities of 28,295 participants in addition to their regular responsibilities, and 1220 subjects had lesions that required further investigation. These primary healthcare providers performed exceptionally well in reducing the risk of oral cavity malignancies.¹¹

Role of Nutrition as a Preventive Strategy

Zinc insufficiency was substantially correlated with poor nutritional status, such as weight loss and low protein content in the blood. Deficit in zinc was significantly linked to squamous cell cancer.¹² Similarly, the active form of vitamin B3 (niacin), nicotinamide, is produced internally primarily by the metabolism of tryptophan, influencing several pathways regulating cell death and survival and taking part in the metabolism of cellular energy.³ Many studies have been conducted on nicotinamide as a safe chemopreventive medication that lowers non-melanoma skin malignancies and actinic keratosis.¹³

Identifying Oral Precancerous Lesions as a Preventive Strategy

In recent times, potentially malignant disorders such as the precancerous lesions of the oral mucosa are considered a set of conditions that need to be detected early. The most prevalent oral mucosal disorders with a high risk of malignant transformation are oral submucous fibrosis, leukoplakia, and erythroplakia. Another potentially malignant illness, oral lichen planus, manifests clinically as papular, reticular, plaque-like, atrophic, erosive, or bullous forms. The probability of

Table 2. Main Outcome Summary of the Review

Included study	Key etiological/aggravating factors/ outcomes
Dailah (2022) ²	Screening is made easy using Mobile health (mHealth) technology
Crossman(2016) ⁴	Role of General Practitioners
Mignogna(2005) ⁹	5 minutes to save a life
Sankaranarayanan et al (2005) ¹⁰	First evidence on the role of early screening
Thampi et al (2022) ¹¹	Health workers may do effective screening during the paucity of dentists.
Kapala A (2024) ¹²	Zinc (nutritional) deficiency may cause cancer
Tosti G et al (2024) ¹³	Nicotinamide is a chemopreventive agent
Scuibba (1999) ¹⁴	Detect Precancerous Lesions
Daftary DK (2010) ¹⁵	Temporal role of tobacco in oral carcinogenesis
Kim SM (2016) ¹⁶	Human papillomavirus causes oral cancer
Ghasemian A et al (2024) ¹⁷	Effects of educational interventions based on the theory of planned behavior
Johnson NW (2011) ¹⁸	Global oral health inequalities leading to oral cancer
Peter TK et al (2022) ¹⁹	Oral microbiome associated with OSCC
de Lima Saintrain MV et al (2018) ²⁰	Tracking soft tissue injuries in the elderly to prevent oral cancer
Rao CV et al. (2018) ²¹	Immunomodulatory Effects of <i>Momordica charantia</i> Extract in Oral Cancer Prevention Research.
Wang WC et al (2016) ²²	Chemopreventive effect of <i>Toona sinensis</i> leaf extract on carcinogenesis.



Figure 2. Dental Health Awareness Camp

malignant transformation is higher in atrophic and erosive subtypes.^{10, 24} A small percentage of individuals were found to have oral leukoplakia, prior to developing oral cancer. Since the majority of leukoplakia cases have no symptoms, preventing the cancer from developing

should be the primary goal of treatment.¹⁴

Tobacco Cessation as a Preventive Strategy:

According to GATS 2, 26.667 million adults in India who are 15 years of age or older, or 28.6% of the population,

currently use tobacco products. 3.7 percent (34.4 million) of adults smoke occasionally, but 24.9 percent (232.4 million) of them smoke every day. Men were 42.4 percent likely to be current smokers, compared to 14.2 percent of women. Among adults, 21.2% in urban regions and 32.5% in rural areas indicated current tobacco use. Within 30 minutes of waking up in the morning, the majority of daily tobacco users (58.5%) start using tobacco.²⁵ Tobacco control must be planned to control the resulting health consequences, which include oral cancerous lesions.¹⁵

Human Papilloma Virus Infection Control as a Preventive Strategy

According to the IARC, there is enough data to link Human Papilloma Virus (HPV) (16 subtypes) to oral malignancies. Clinically, HPV-related tumors often present as strawberry-shaped exophytic lesions, usually on the tonsil or the base of the tongue. Most display cystic alterations in the metastatic neck lymph nodes and poorly differentiated histologic features. It is unknown if HPV plays a part in the malignant transformation of precancerous lesions. However, HPV infection can occur in the chronic mucocutaneous form of oral lichen planus.¹⁶

Educational Interventions as a Preventive Strategy

The theory of planned behavior is a helpful model for promoting behavioral change. A randomized controlled trial was carried out in 2022 to investigate the impact of tobacco-use-prevention behavior-based educational interventions on tobacco smoking behavior and oral cancer knowledge in an adult Iranian population. There were 400 healthy participants in the trial. The study's implementation involved twenty urban health centers in Tehran, Iran. Two intervention groups were randomly assigned to the medical facilities, PowerPoint and WhatsApp. A pamphlet was distributed to each participant in the PowerPoint (PP) group during a 20-minute PP presentation to educate the audience. The WhatsApp (WA) Group was educated using images and messages on WhatsApp. A structured questionnaire was employed during the trial and at the one- and three-month follow-ups. The results were assessed in terms of knowledge of the destructive effects of tobacco smoking behavior, which was recorded to be reduced in both groups.¹⁷

Inequality Reduction as a Prevention Strategy

Oral cancer is considered to be a disease of the poor. Inequality reduction is more likely to be efficacious with a whole-of-society approach by policy-makers. Basic research aims to understand the individual vulnerability and the genetic factors involved in the occurrence of cancers. This can translate into successful therapies that should be pursued by the poor and the underprivileged.¹⁸

Controlling Oral Microflora as a Preventive Strategy

Over the past ten years, research on the relationship between oral health and the human oral microbiome has become increasingly popular. To find potential biomarkers that could enable an earlier diagnosis and a better prognosis for individuals who have oral cancer, this impetus has spurred a search for correlations between the oral microbiota and the disease. Three categories of data were gathered from the studies: gene abundance data, projected functional pathway data, and bacteriome data down to the genus level. These data revealed various microbial taxa, such as *Fusobacterium*, that may be connected to the state of oral cancer. Furthermore, the adenosine tri-phosphate(ATP)-binding cassette, subfamily B, bacterial gene K06147 was overexpressed in OSCC samples by examining gene abundance data.¹⁹

Monitoring Soft Tissue Damage as a Preventive Measure

Monitoring soft tissue damage regularly and referring older adults with suspected lesions that may turn malignant should be included as oral cancer identification methods in any healthcare unit for targeted prevention. Furthermore, healthcare providers should educate older adults on the importance of regular preventive dental visits for accurate examinations.²⁰

Chemoprevention of Oral Cancer: A Case Under Study

Chemoprevention is the use of certain drugs to avoid the formation, growth, or return of cancer.

A clinical research study is being conducted to find out if erlotinib hydrochloride can shield those who have a high risk of oral cancer from developing it. This drug's safety and its effects on various body cells have also been investigated.^{12,26} The purpose of erlotinib hydrochloride is to inhibit the activity of an enzyme present on the surface of many tumor cells, which may regulate the growth and survival of tumors. This could prevent cancers from spreading.

The use of celecoxib(CXB) may prevent or treat head and neck cancer. Celecoxib has been shown to have the ability to treat cancer by preventing cancer cells from proliferating through apoptosis; however, it is yet unknown how this medication would affect the mobility of cancer cells and the epithelial-mesenchymal transition. Retrospective cohort research demonstrated a correlation between oral cancer prevention and the increase in CXB dosage and duration of administration. The results offer an alternate method of preventing the development of oral cancer by using CXB.²⁷ However, no results have been posted.²⁸

Use of Artificial Intelligence as a Preventive Strategy

Another successful preventive strategy is using a probabilistic neural network and general regression neural network (PNN/GRNN) data mining model for the early detection and prevention of oral cancer. To categorize

instances as malignant or non-malignant, the model considers all characteristics related to clinical symptoms and history. The algorithm then tries to forecast the specific cancer type, stage, and extent, using characteristics related to symptoms, physical examination, and research. Additionally, the model anticipates a patient's survivability based on treatment and follow-up information. Lastly, a comparison is made between the performance of the PNN/GRNN model and various categorization models. Because the PNN/GRNN model has an 80% classification accuracy, it is superior for early oral cancer detection and prevention.¹³

Practical experiences with clinical decision support system (CDSS) applications across several cancer types have demonstrated the great potential of machine learning techniques for intelligent and accurate data management and improved diagnosis in oral cancer (OSCC).²⁹

Preventive Nature of Some Herbs

Bitter melon extract has recently drawn much attention due to its anticancer activity against various cancers. It has been demonstrated to have potential therapeutic effects in stopping or postponing the development of squamous cell carcinoma from oral dysplasia.²¹

Toona sinensis leaf extract has also been shown to have anti-tumor effects on cancer cell lines. A study aimed to investigate the chemopreventive potential of the leaf extract suggested that it might be effective in preventing oral cancer.²²

Cancer Vaccines

Can prevention of oral cancer ever be achieved with "cancer vaccines?" It is true that commercially available vaccines against the human papillomavirus and hepatitis B can prevent liver and cervical cancer, respectively. However, both vaccines are designed to prevent viruses—albeit ones connected to cancer—rather than malignant cells. Nevertheless, several investigations conducted on animal models indicate that vaccinations directed against antigens directly expressed by tumors may be able to stop cancer growth, as depicted in Figure 3.

Limitations of the Scoping Review

Some clinically relevant criteria for suspecting oral cancer, for example, Mallampatti grading for Tonsils,³⁰ and their link to the diagnosis of any oral cavity malignancy are not recorded, as they were not detected during the database search. Furthermore, only four databases were searched during this scoping review. The literature search produced several duplicate findings, including cancer patients who underwent head and neck radiation therapy and whose soft tissues was altered, both temporarily and permanently, in addition to experiencing acute and long-term abnormalities in their sensory perception. Radiation-induced xerostomia in chemotherapy and radiotherapy

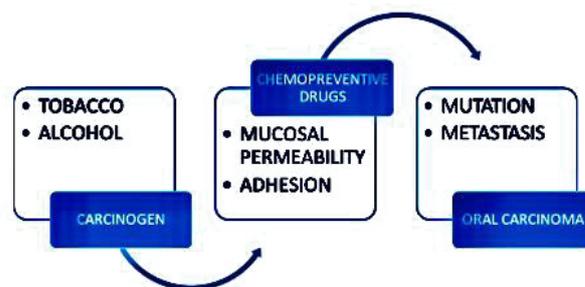


Figure 3. Role of chemo preventive drugs/ cancer vaccines

is recorded as an undesirable side effect with adverse consequences outside cancer treatment, which was again a frequent duplicate in the search method. There is no mandatory need for evidence generation using statistical analysis such as odds ratio for a scoping review.

Conclusion

Dentists have a role in providing individualized treatment (precision dental medicine) for oral squamous cell carcinomas at an early stage, even before the patient perceives symptoms or a general physician refers them. A referral from a dentist is more significant than one from a physician. Dental students must be taught and trained adequately for early diagnosis and for increasing longevity.

Competing Interests

The authors declare that they have no known competing financial interests or personal relationships that could influence the work reported in this paper.

Data Availability Statement

All data analyzed are included in the present article.

Ethical Approval

Since this is a review paper of works that have already received ethical approvals, no ethical approval has been obtained.

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