



Review Article

Oral Cancer Screening: Insights into Epidemiology, Risk Factors, and Screening Programs for Improved Early Detection



Amit Kumar Jain*

Bhagwan Mahaveer Jain Hospital, Bengaluru, Karnataka, India

Received: June 30, 2023 | Revised: February 17, 2024 | Accepted: April 24, 2024 | Published online: June 18, 2024

Abstract

Early detection of oral cancer is crucial for improving prognosis, increasing survival rates, and reducing treatment-related morbidity, considering the high mortality rate associated with this condition. However, the conventional approach within communities has led to a growing exploration of different screening methods to detect potentially malignant oral disorders, with particular emphasis on imaging and artificial intelligence and their integration with conventional approaches. The article reviewed literature on oral neoplasms and early cancer detection from databases like Medline, Google Scholar, and Web of Science, mainly from 2001 to 2023. This review aims to shed light on the potential of these technologies, new ideas, and methods in improving the accuracy and effectiveness of oral cancer screening, ultimately leading to earlier detection and more successful prevention strategies, which are unmet needs, especially in underdeveloped and developing nations. Conventional visual examination remains fundamental for oral cancer screening, while imaging, biomarkers, and artificial intelligence assisted approaches show potential as adjunctive tools but require further clinical validation.

Introduction

Cancer is a complex and devastating disease characterized by the uncontrolled growth and spread of abnormal cells in the body. It can affect various organs and tissues, leading to significant health challenges and, in some cases, life-threatening conditions. Head and neck cancer ranks as the sixth most prevalent form of cancer worldwide, with a higher incidence observed in South-central Asia, where it stands as the third most common cancer type in that region.¹ Oral squamous cell carcinoma is the predominant malignancy among reported cases of head and neck cancers, posing a growing health concern worldwide.^{1,2}

Oral cancer, often overlooked or underestimated, refers to the abnormal growth of malignant cells in the mouth's tissues, including the lips, tongue, gums, and cheeks.² It is a disfiguring and life-threatening condition, with a discouraging five-year disease-specific survival rate of 50% to 60%. Diagnosis of oral cancer commonly occurs in advanced stages (approximately 60% of patients present with

advanced-stage disease at the initial diagnosis), remaining a formidable challenge in head and neck oncology. Usually, patients bear a significant portion of the responsibility for delays in diagnosis. However, it is essential to state that diagnostic delays can also arise from a medical approach that sometimes, fails to suspect an oral malignancy, leading to delayed or inadequate diagnosis and treatment.²⁻⁴

The strategy for oral cancer should encompass preventive and control measures, such as regular screening for early identification, providing chances for assessing oral lesions (via proactive searches such as home visits or targeted campaigns), ensuring follow-up for suspected cases with the option of establishing referral services if needed and fostering collaborations between universities and other entities for prevention, diagnosis, treatment, and rehabilitation.⁵

Early detection of oral malignancy is crucial for improving prognosis, increasing survival rates, and reducing treatment-related morbidity, considering the high mortality rate associated with this condition. By promptly identifying oral cancers, patients have a higher chance of receiving timely interventions, leading to more effective treatment outcomes and reduced complications. Emphasizing early detection and anticipating diagnosis plays a significant role in improving overall prognosis and minimizing treatment impact on patients' well-being.⁴

Presently, the standard practice for diagnosing potentially malignant diseases and oral squamous cell carcinoma (OSCC) involves routine oral examination, including visual and tactile inspection of accessible oral structures along with tissue biopsy.

Keywords: Oral cancer; Oral potentially malignant disorders; Prevention; Screening; Early detection; Tobacco; Artificial intelligence.

***Correspondence to:** Amit Kumar Jain, Bhagwan Mahaveer Jain Hospital, Bengaluru, Karnataka 560052, India. ORCID: <https://orcid.org/0000-0002-7166-2023>. Tel: +91-9475622246, E-mail: 20akjain@gmail.com

How to cite this article: Jain AK. Oral Cancer Screening: Insights into Epidemiology, Risk Factors, and Screening Programs for Improved Early Detection. *Cancer Screen Prev* 2024;3(2):95–103. doi: 10.14218/CSP.2023.00029S.

Nonetheless, this approach has inherent limitations such as sampling bias, potentially leading to underdiagnosis or misdiagnosis, particularly in cases involving multifocal lesions.⁶

Recognizing the significant disease burden of oral cancer and the conventional approach within communities, there has been a growing exploration of different screening approaches to detect oral potentially malignant disorders (OPMDs) and invasive cancer. Several clinical trials have investigated these screening methods' potential in identifying and diagnosing OPMDs and invasive oral cancer.⁷ The aim is to develop more effective and efficient strategies for early detection and intervention, ultimately improving patient outcomes and reducing the impact of this devastating disease. The objective of this review is to discuss screening methodologies for early detection and prevention of oral cancer, emphasizing imaging, artificial intelligence (AI), and their integration with conventional approaches. Exploring these advancements aims to shed light on the potential of these technologies in improving the accuracy and effectiveness of oral cancer screening, ultimately leading to earlier detection and more successful prevention strategies.

This review was performed based on articles focused on epidemiology, screening techniques, and various models for detecting oral cancer at its early or precancerous stages, sourced from international databases such as Medline, Google Scholar, and Web of Science, with a primary focus on literature published between 2001 and 2023; earlier relevant studies were also included where appropriate. The search keywords used were: "screening", "prevention", "early detection", "tobacco", "oral cancer", "oral potentially malignant disorders", "head and neck cancer" and "artificial intelligence". Articles concerning the management of oral neoplasms or head and neck cancer were excluded as this review aims to shed light on technologies, new ideas, and methods that improve the accuracy and effectiveness of oral cancer screening and early detection.

The overview of oral cancer

Epidemiology

The effect of cancer on the population can be effectively evaluated by considering key indicators such as the incidence rate, survival rate, and mortality rate within the specific population. Analyzing these metrics provides healthcare professionals and researchers with valuable insights into the prevalence and impact of cancer, enabling better resource allocation and implementation of targeted prevention and treatment strategies.¹

Epidemiological studies focusing on oral cancer encounter complexities arising from various anatomical sub-sites, leading to diverse reporting practices. The classification and grouping of oral cancer exhibit substantial variations, posing challenges for comparative evaluations within different populations. These discrepancies in reporting and classification hinder the ability to draw comprehensive and standardized conclusions, impacting our understanding of the disease on a global scale.⁸ In 2018, Conway *et al.*,⁹ along with the International Classification of Disease for Oncology, proposed a method to distinguish oral cancer from oropharyngeal cancer on the basis of the site of malignancy.

Based on the aforementioned classifications, recent data from GLOBOCAN 2020 revealed approximately 377,713 new cases of oral cancer detected in both sexes, resulting in approximately 177,757 deaths worldwide. Most oral cancer cases were reported in Asia, accounting for about 248,360 cases, representing 65.8% of the total cases in 2020, followed by Europe (17.3%), North America (7.3%), the Caribbean (4.7%), and Africa (3.8%). However, the distribution

of mortality statistics showed some variations, with the highest number of deaths occurring in Asia (74%), followed by Europe (13.8%), Africa (4.6%), the Caribbean (4.2%), and North America (2.8%).¹⁰ These regional differences in incidence and mortality rates highlight the importance of understanding unique challenges and factors contributing to oral cancer in different parts of the world.

India has a high incidence of oral cancer, attributed to cultural, ethnic, and geographical factors, along with prevalent addictive habits. Among men, oral cancer ranks as the most diagnosed cancer and has the highest incidence. Among women, it ranks as the third most prevalent cancer in the country.¹¹ In India, there are approximately 77,000 new cases of oral cancer reported each year, resulting in around 52,000 deaths, indicating the substantial burden of this disease.¹² These figures represent approximately one-fourth of global oral cancer cases. According to the report "Cancer Incidence in Five Continents - Volume VIII," Bhopal, one district in India, has the highest Age-Adjusted Rate (AAR) for both tongue cancer (10.9 per 100,000) and mouth cancer (9.6 per 100,000) globally. Additionally, the urban registry of Ahmedabad exhibits a high AAR of 9.3 per 100,000 for tongue cancer, with other urban cancer registries in India reporting AARs ranging from 3.4 to 6.0.¹³ In a similar study conducted in the Mainpuri district of India, the annual incidence rate of oral cancer was reported as 21.4 cases per 100,000 individuals.¹¹

A study conducted by Byakodi *et al.*¹⁴ in 2011 evaluated the prevalence of oral cancer in the Indian population over two years in the Sangli district. The study found that the overall prevalence of oral cancer in the study population was 0.3%. However, when analyzing habits of tobacco and alcohol consumption, the prevalence increased to 1.12%. Most reported cases were in the advanced stage and had full-blown malignancies, indicating that individuals in rural areas do not seek medical care until the lesions become symptomatic or reach a significant size. Factors such as low literacy rates and lack of awareness among patients were considered additional contributors to delayed medical attention. This suggests a need for increased education and awareness campaigns targeting the rural population to promote early detection and timely medical intervention. By addressing these factors, it is possible to improve the prognosis and outcomes for individuals affected by oral cancer in the Indian population.

The National Cancer Institute estimates that in 2023, there will be 54,540 new cases of oral cavity and pharynx cancer in the United States (Fig. 1). Figure 2 represents the predicted sex-specific distribution of the above cases.^{15,16}

Characteristics

Oral cancer poses a significant public health challenge, with an increasing trend in its incidence, particularly among young men and women. Over 90% of oral cancers are classified as OSCCs. In addition to OSCCs, the oral cavity can also be affected by tumors originating from the minor salivary glands, melanomas, and lymphomas.⁴ Even though OSCC can manifest in various locations, there are specific areas where it is more frequently observed. The most prevalent sites for OSCC development are the tongue and the floor of the mouth. Additionally, it can affect the buccal mucosa, retromolar area, gingiva, soft palate, and, although less commonly, the posterior part of the tongue and hard palate. Pain is a prevalent symptom among oral cancer patients, accounting for 30–40% of their primary complaints. However, pain typically becomes noticeable only when the lesions have grown considerably in size, prompting patients to seek medical assistance. As a result, early-stage carcinomas often go unnoticed since they do not cause any symptoms. In more advanced and larger lesions, symptoms can range from mild discomfort to se-

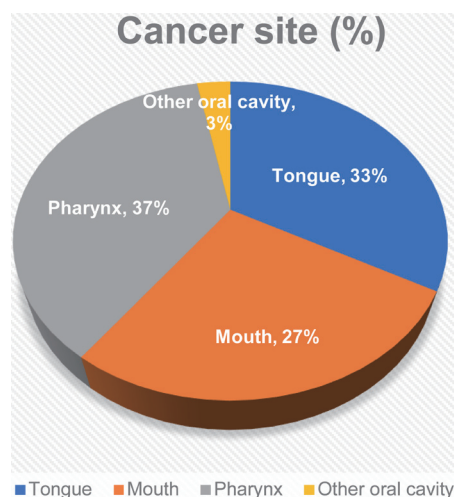


Fig. 1. Distribution of estimated new oral cavity and pharynx cancer cases by anatomic site in the United States, 2023.

vere pain, particularly in the tongue. Additional symptoms may include ear pain, bleeding, tooth mobility, breathing difficulties, speech problems, dysphagia, challenges with prosthesis usage, trismus, and paraesthesia.¹⁷ The clinical presentation of OSCC is typically distinctive, often starting from red or red and white lesions, further advancing to ulceration and lumps. The advanced stage raises a strong suspicion of malignancy. However, in the early stages, there is a greater possibility of misdiagnosis. Therefore, it is imperative to confirm the diagnosis through a biopsy and histopathological examination rather than relying solely on clinical characteristics, which might be insufficient for an accurate diagnosis of OSCC.¹⁸

Risk factors associated with oral cancer

Individual predispositions, genetic characteristics, and exposure to carcinogens resulting from lifestyle behaviors contribute to the

majority of oral cancer cases and related deaths. Approximately 20–30% of cases are attributed to tobacco/bidi smoking, while nearly 50% in men and almost 90% in women are linked to frequent betel quid chewing without tobacco in regions with high chewing prevalence. Heavy alcohol consumption is responsible for 7–19% of cases, and micronutrient deficiency accounts for 10–15% of cases. Human papillomavirus (HPV) infection, primarily but not exclusively associated with sexual behavior, contributes to around 3% of cases. It is important to note that exposure to multiple risk factors has a synergistic effect, further increasing the risk of developing oral cancer.¹⁹

Recent clinical and scientific studies have shed light on the oncogenic role of various factors in oral cancer development, such as the oral microbiome, mucosal inflammation, and oral mucosal trauma caused by sharp teeth, implants, faulty restorations, and prosthetic devices. The presence of specific microbial communities in the oral cavity and chronic inflammation of the oral mucosa have been linked to an increased risk of oral cancer.²⁰

In the case of lip cancer, actinic ultraviolet (UV) radiation, particularly UV-B, plays a significant role. Prolonged exposure to UV radiation, often from sunlight, can damage the DNA in lip cells and contribute to cancer development.²¹ Certain genetic conditions also predispose individuals to a higher risk of oral cancer. For example, individuals with Xeroderma pigmentosum, Fanconi's anaemia, and Ataxia-telangiectasia have genetic abnormalities that affect DNA repair mechanisms, leading to an increased susceptibility to oral cancer.²²

Understanding these factors, including the oral microbiome, mucosal inflammation, oral mucosal trauma, UV radiation, and genetic conditions, helps identify individuals at higher risk for oral cancer. This knowledge guides preventive measures, early detection strategies, and personalized treatment approaches to reduce the incidence and mortality associated with oral cancer.

Prevention and detection of oral cancer

Despite advancements in oral cancer therapy, the prognosis for OSCC remains unfavorable. Therefore, the focus should be on oral

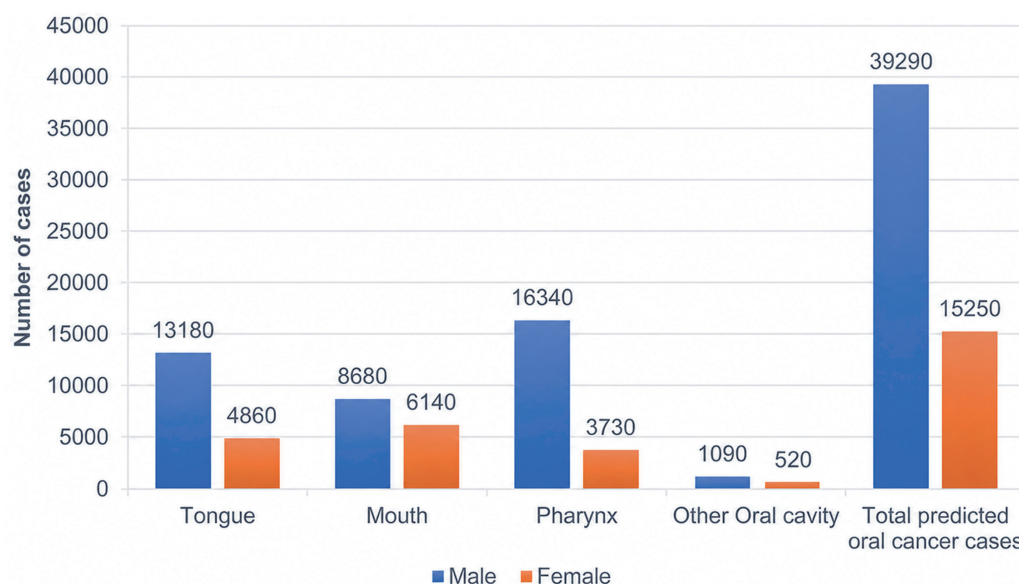


Fig. 2. Estimated numbers of new oral cavity and pharynx cancer cases by sex and anatomic site in the United States, 2023.

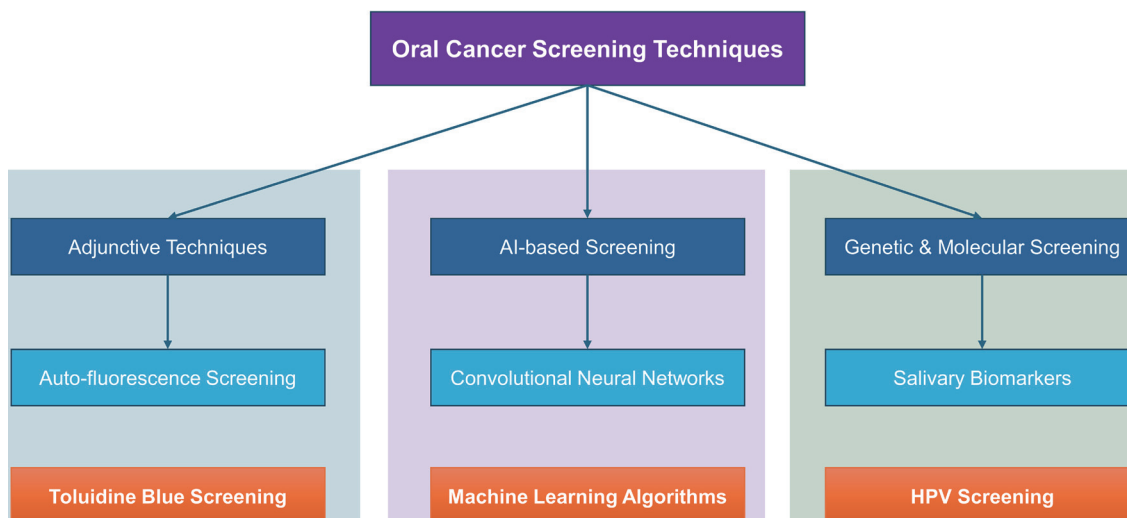


Fig. 3. Oral cancer screening techniques. AI, artificial intelligence; HPV, human papillomavirus.

cancer prevention. Primary prevention strategies, such as reducing tobacco, alcohol, and betel quid consumption, have demonstrated effectiveness in reducing oral cancer occurrences. Secondary prevention focuses on screening methods to facilitate early oral cancer identification. Promising evidence from a significant primary intervention trial conducted in India suggests that the chances of oral precancerous lesions progressing into malignancy can be reduced by encouraging individuals to decrease their tobacco and betel consumption. Additionally, dietary modifications and potentially beneficial micronutrients like vitamins C, A, and E may help lower the risk of oral cancer.²³ Oral cancer researchers widely concur that early detection of oral carcinoma significantly enhances the chances of a successful cure while minimizing the impact on appearance and function. Clinical examination and biopsy are crucial for the early detection of premalignant and early-stage oral cancers. To enhance screening effectiveness, it is recommended to focus on high-risk sites, including the floor of the mouth, the ventrolateral surface of the tongue, and the soft palate. Treated oral cancer patients should undergo more frequent examinations to monitor the development of secondary tumors. Family members of oral cancer patients are also at a higher risk and should undergo frequent examinations as well. Regardless of the screening method used, a positive screening result must be confirmed through biopsy. To combat the high morbidity and mortality rates associated with oral cancer, a public awareness program is necessary. This program should emphasize the importance of at least one annual dental examination for recognition of warning signs of oral cancer and raising awareness about the risks of tobacco and alcohol use.²⁴ Early detection allows for prompt intervention and appropriate treatment, leading to improved chances of successful outcomes. It also provides an opportunity to educate individuals about risk factors, lifestyle modifications, and the importance of regular follow-ups.

Oral cancer screening

Oral cancer screening is a preventive measure designed to identify early signs of oral cancer or precancerous lesions in the mouth. The screening criteria aim to identify individuals with oral cancer or OPMD who are at risk of developing cancer. It's important to

note that a screening test or examination is not diagnostic in nature. Instead, the objective is to detect any abnormal tissue or suspicious lesions that may indicate the presence of oral cancer.^{25,26} Screening must detect disorders or malignancies before symptoms arise to reduce the mortality of the screened population.

There are different methods and techniques that may support oral cancer screening or the adjunctive assessment of suspicious oral lesions (Fig. 3).

Visual examination

One common approach is visual inspection, where a dental or healthcare professional carefully examines the oral cavity for any visible signs of abnormalities. They look for unusual color changes, lumps, sores, or patches that may indicate potential cancerous or precancerous conditions.²⁶ This method has a sensitivity of 85% and a specificity of 97%.²⁷

Toluidine blue-staining

Toluidine blue staining is a cost-effective, non-invasive technique widely used as an adjunct in diagnosing malignant and pre-malignant lesions of the oral cavity. This method involves the application of a 1% aqueous solution of toluidine blue to the suspected lesion for 30 s. Prior to this application, 1% acetic acid is used to remove the salivary and bacterial pellicle from the area. The dye selectively stains areas of dysplastic epithelium, resulting in a distinctive royal blue coloration. The staining pattern is then carefully evaluated to assess the presence of abnormal cells or potential cancerous changes. This procedure is simple, quick, and provides valuable information to aid in the diagnosis and management of oral lesions.^{4,28}

While toluidine blue staining is valuable in oral cancer screening, its specificity is relatively low. This is because various types of mucosal ulcerations, including those caused by trauma, inflammation, or pre-neoplastic conditions, can bind toluidine blue and produce a positive result. Therefore, a positive toluidine blue staining does not necessarily indicate the presence of malignant or pre-malignant lesions. Furthermore, studies have shown a correlation between toluidine blue positivity and a worse prognosis. Lesions that exhibit positive staining tend to demonstrate a higher likelihood of growth and are more likely to progress into cancer com-

pared to lesions that show negative staining. This suggests that a positive toluidine blue result may indicate a higher risk or a more advanced stage of the disease.²⁹

Applications of this method include identifying epithelial dysplasia, early invasive carcinomas, delineating neoplastic epithelium margins, evaluating tumor recurrence post-surgery or radiotherapy, defining areas of cancer activity, screening oral lesions in high-risk population groups, and assisting in intraoperative procedures for carcinoma control. Its benefits include painlessness, affordability, ease of application, rapid results, and high sensitivity. However, drawbacks encompass the potential for false-positive or false-negative outcomes and limited specificity.⁵

Therefore, while toluidine blue staining can be a useful aid in the diagnosis and management of oral lesions, its interpretation should be done in conjunction with other clinical findings and diagnostic tests to ensure accurate assessment and appropriate treatment decisions.

Auto-fluorescence imaging

Autofluorescence imaging is an adjunctive tool that can provide valuable insights into oral lesions, complementing clinical examinations using white light. While visual and tactile examination remains the primary method for diagnosing oral cancer, autofluorescence imaging assists in identifying lesions that may require biopsy. Autofluorescence imaging takes advantage of the natural fluorescence emitted by tissues when excited with specific light wavelengths. Endogenous fluorophores, such as collagen, elastin, keratin, flavin adenine dinucleotide, and nicotinamide adenine dinucleotide, contribute to healthy tissue autofluorescence. In dysplasia and cancer, alterations in tissue fluorescence occur, resulting in a loss of green fluorescence and a darker appearance of the mucosa.³⁰ Conversely, normal mucosa typically exhibits light-green fluorescence. This change in fluorescence is attributed to disruptions in the distribution of elements responsible for autofluorescence in healthy tissues. Over the years, autofluorescence imaging devices have been developed and marketed to capture and analyze these fluorescence patterns.³⁰

It is important to note that autofluorescence imaging should be used as an adjunct to visual and tactile examination, not as a replacement. While this technique offers advantages such as high sensitivity (estimated at 91%) and non-invasiveness, its main limitation is its relatively low specificity (estimated at 58%). This is because benign conditions, including inflammatory diseases, can also cause changes in tissue autofluorescence that resemble those observed in malignant and pre-malignant conditions.^{4,31}

In summary, autofluorescence imaging provides additional information aiding oral lesion diagnosis with its high sensitivity and non-invasive nature. However, its specificity limitation arises from similar autofluorescence changes between benign and malignant conditions. Therefore, a comprehensive evaluation combining clinical examination, autofluorescence imaging, and other diagnostic modalities is essential for accurate diagnosis and appropriate management decisions.⁴

Optical coherence tomography

In an optical coherence tomography scanning system, a low-coherence light is coupled with a fiber-optic interferometer. This process efficiently captures two- and three-dimensional images with micrometer resolution from the light-scattering biological tissue. Hence, it is a valuable diagnostic modality since it offers high-resolution real-time images with less acquisition time, and, most importantly, it is non-invasive in nature. In OPMD, it demonstrates

sensitivity and specificity of approximately 90%.^{32,33}

Salivary biomarkers

Salivaomics is a field that focuses on analyzing biological molecules in saliva, which can provide insights into various human disease processes. It encompasses different approaches, such as salivary genomics/epigenomics, proteomics, transcriptomics, metabolomics, and microbiomics, all of which have the potential to identify biomarkers for disease detection.³⁴ In the case of oral cavity and oropharynx cancers, the proximity of saliva to these areas, along with the ease of collecting saliva or oral rinses (referred to as “liquid biopsy”), makes it feasible to utilize saliva as a biofluid for oral cancer screening.²⁶

In recent years, there has been a significant increase in research aimed at identifying potential salivary biomarkers for oral cancer. These studies often involve testing individual biomarkers or combinations of biomarkers in case-control studies. However, further research is necessary to evaluate and enhance the sensitivity and specificity of these testing techniques. It is crucial to determine whether these biomarkers can serve as reliable indicators for clinicians to assess the potential presence or progression of malignant transformation in the oral mucosa.

Continued efforts in salivaomics hold promise for effective screening tools for oral cancer. By harnessing the unique molecular information present in saliva, researchers aim to refine and validate the use of salivary biomarkers, paving the way for improved early detection and monitoring of oral cavity and oropharynx cancers. Further studies are needed to establish the clinical utility and reliability of these biomarkers, ultimately providing clinicians with valuable tools for assessing the potential risk or presence of malignant transformation in the oral mucosa.^{34,35}

HPV screening

HPV infection, recognized as the most prevalent sexually transmitted infection, has been implicated in the development of head and neck squamous cell carcinomas and OSCC.³⁶ For individuals with clinically normal oral mucosa, a recommended diagnostic approach for screening is the collection of a cytological sample using a mouthwash technique. This involves rinsing the mouth with either a 10 ml solution of cetylpyridinium chloride or a sterile saline solution. The collected sample is then promptly examined in a laboratory using molecular biology techniques, such as SPF10-LiPA, to identify the specific viral species or types present.^{36,37}

Tang *et al.* conducted a screening study in 2020, involving 665 individuals who were considered “cancer-free,” both saliva and oral rinse samples were collected to test for HPV-16 DNA. The study aimed to identify HPV-positive individuals and monitor them over time. Participants who tested positive for HPV-16 were followed up and retested every three to six months. Among HPV-positive individuals, three subjects exhibited persistent HPV-16 infection for over 30 months.³⁸

Performing regular screenings using this diagnostic approach can aid in early detection and intervention, enabling appropriate management and treatment strategies for individuals at risk of developing HPV-associated cancers. The use of molecular biology techniques, such as SPF10-LiPA, ensures accurate identification and characterization of HPV viral species, enhancing the reliability of the screening process.^{36,37} Further research and advancements in molecular diagnostics continue to refine and expand the understanding of HPV-related diseases. Screening methods involving cytological samples obtained through mouthwash techniques, coupled with molecular biology techniques, provide valuable insights

into the presence and types of HPV infections, facilitating early detection and targeted management of HPV-associated cancers.^{4,36} This approach has a moderate sensitivity of 72% and a good specificity of 92% in HPV-related head and neck squamous cell carcinomas.³⁹

AI-based screening

AI techniques are gaining significant attention as a means to enhance image-based diagnosis of oral cancer. Two subsets of AI, machine learning, and deep learning, are utilized for intelligent image analysis, depending on available data sets and specific applications. Compared to manual interpretation of medical images, AI offers advantages such as increased efficiency, reduced time consumption, decreased dependence on specialist expertise, and improved accuracy.⁴⁰

A milestone in AI-assisted oral cancer screening was reported by Birur *et al.* in 2022. They validated a mobile point-of-care system combining oral imaging with deep learning in 5,025 individuals. The system achieved sensitivities of 82%–87% and showed potential for assisting frontline health workers in identifying suspicious oral lesions.⁴¹

The integration of AI into image-based diagnosis holds great potential for improving efficiency, accuracy, and cost-effectiveness in healthcare. By leveraging AI algorithms to analyze medical images, clinicians can benefit from enhanced decision support and screening capabilities. Some applications and advantages of AI in oral cancer screening include:

- **Screening high-risk populations:** AI can assist in identifying individuals at higher risk of developing oral cancer, enabling targeted screening programs for early detection.
- **Early diagnosis in remote regions:** AI can be particularly useful in remote areas with limited access to healthcare facilities. It can aid in the early diagnosis of oral cancer, allowing timely intervention and treatment.
- **Precise analysis of large datasets:** AI algorithms efficiently analyze vast data, identifying patterns and markers associated with oral cancer for more accurate diagnoses and treatment decisions.
- **Detection and classification of lesions:** AI can detect and classify cancerous lesions by interpreting images of the oral mucosa, and distinguishing between normal tissue, precancerous conditions, and cancerous growths.
- **Multicenter study facilitation:** AI systems are easily deployable across multiple centers, allowing for standardized analysis and comparison of data in large-scale studies.
- **Automated learning and outcome generation:** AI systems can learn from data without human intervention, automating processes and combining variables to provide valuable outcomes and insights.
- **Decision support for clinicians:** AI can guide clinicians in decision-making by analyzing various factors such as history, geography, risk factors, imaging features, and omics data to generate risk assessments and treatment recommendations.
- **Enhanced accuracy in pathology:** AI systems can assist expert pathologists in delivering superior results with minimal diagnostic errors, improving the accuracy and reliability of pathology assessments.
- **Prediction of malignant transformation:** AI algorithms can help predict the likelihood of OPMDs transforming into malignant lesions, aiding in treatment planning and patient management.
- **Biomarker detection:** AI can accurately identify and analyze specific biomarkers associated with oral cancer, contributing to

targeted therapies and personalized treatment approaches.

- **Lymph node metastasis prediction:** AI models can analyze imaging data and clinical features to predict the likelihood of lymph node metastasis in oral cancer patients, assisting in treatment planning and prognosis assessment.
- **Support in treatment planning:** AI systems can provide valuable insights and recommendations to clinicians in treatment planning, considering various factors such as patient characteristics, tumor characteristics, and treatment outcomes.^{40,42}

Overall, the application of AI in oral oncology holds great promise for improving screening, diagnosis, treatment, and patient outcomes. Continued research and development are essential to harnessing the full potential of AI in oral cancer care by refining AI techniques, validating their effectiveness, and expanding their applications for advanced medical diagnosis and patient care.

Oral cancer screening program

An oral cancer screening program is a systematic approach aimed at detecting and diagnosing oral cancer at an early stage. These programs typically involve a series of screening procedures and interventions to identify individuals who may be at risk for oral cancer or who may already have early signs of the disease. The goal is to detect oral cancer in its early stages when treatment is more effective and can significantly improve outcomes.²⁵

A significant challenge in oral cancer management is the delayed presentation of patients, often at an advanced stage of the disease. Many individuals affected by oral cancer tend to overlook or ignore the early signs and symptoms, resulting in late diagnosis and treatment initiation. The lack of awareness regarding cancer-related symptoms and the misconception that cancer does not commonly occur in the oral cavity contribute to this issue.

In a collaborative effort from Morikawa *et al.*⁴³ (2021, Tokyo Dental College) and a local dental association, an oral cancer screening program was conducted for 27 years from 1992 to 2018. The study also included a 13-year opportunistic screening period from 2006 to 2018. The findings of the study demonstrated the effectiveness of both the countermeasure and opportunistic screening systems. The results indicated that the opportunistic screening approach was particularly advantageous in several factors. Firstly, it attracted a larger number of examinees compared to the countermeasure screening system. This suggests that the opportunistic approach had a higher participation rate, potentially due to the convenience of selecting a preferred time and date for the screening at a nearby general practitioner's dental clinic. Secondly, the gender ratio of participants was more balanced in the opportunistic screening system, indicating the successful engagement of both male and female individuals in the screening process. Additionally, the close examination rate was significantly lower in the opportunistic screening system than in the countermeasure screening system. Furthermore, the opportunistic screening system exhibited a higher detection rate for OPMDs compared to the countermeasure screening system. This highlights the effectiveness of the opportunistic approach in identifying early signs of oral cancer and related disorders. Overall, the study findings provide evidence supporting the value of both the countermeasure and opportunistic screening systems for oral cancer. The opportunistic screening approach, with its flexibility and accessibility through general practitioners' dental clinics, demonstrated advantages in terms of participant numbers, gender representation, close examination rates, and OPMD detection rates. These insights contribute to ongoing efforts to optimize oral cancer screening programs and improve the overall manage-

ment of oral health.

Implementing of cancer screening programs is hindered by fragmented, low-resource settings lacking workforce and technical facilities—common in developing countries—underscoring the need for an organized healthcare system as a primary requirement. The main barriers to the opportunistic screening system are out-of-pocket healthcare spending by private dental practitioners, lack of training (for examination and biopsy), and absence of a proper referral system with a follow-up mechanism along with significant variations in risk factors, socioeconomic attributes, health-seeking practices, health literacy levels, and healthcare accessibility among states. It can be countered by tailored cancer prevention strategies based on regional diversities by involving dental schools in the development of proper referral and follow-up facilities.^{44,45}

Screening for oral cavity cancer and OPMDs using risk prediction models has been recognized as a cost-effective approach.⁴⁶ A risk prediction model has been developed for head and neck cancers, including oral cancer, which takes into account factors such as age, gender, race/ethnicity, education level, and cigarette smoking/alcohol consumption.⁴⁷ However, this model does not specifically consider OPMDs. To address this gap, a group in Sri Lanka has developed a risk prediction model specifically for OPMDs, utilizing field surveys to study the association between lifestyles and the development of OPMDs.⁴⁸

In addition to these models, there has been a focus on developing a risk prediction model for future screening of oropharyngeal cancers in the United States. This model incorporates various factors such as age, sex, race, smoking, alcohol use, lifetime sexual partners, and oncogenic HPV status.⁴⁹ By considering these risk factors, the model aims to identify individuals who are at a higher risk of developing oropharyngeal cancers, enabling targeted screening efforts for early detection and intervention.

The utilization of AI techniques in advancing image-based diagnosis is gaining popularity, primarily through deep learning and machine learning. Deep learning networks utilize layers of artificial neural networks to autonomously generate categories based on their identification of differences (edges) within neural network layers exposed to extensive data points. In contrast, machine learning algorithms typically require accurately categorized data input. The efficiency of automated cancer diagnosis has notably improved, thanks to the development and refinement of convolutional neural networks.⁶

Improving public awareness about oral cancer and its symptoms is crucial in addressing this issue. Healthcare providers, dental professionals, and public health organizations play a vital role in disseminating information about oral cancer and promoting early detection. By conducting community outreach programs, organizing awareness campaigns, and integrating oral cancer education into routine dental visits, the public can be better informed about the signs and symptoms of oral cancer. Educational initiatives should focus on educating individuals about the risk factors associated with oral cancer, such as tobacco and alcohol use, HPV infection, and poor oral hygiene.

Limitations

This narrative review has several limitations. The literature search was not systematic, and no formal assessment of study quality was performed. In addition, the included evidence involved heterogeneous populations and, in some studies, oral, oropharyngeal, and broader head and neck cancers, which may limit the generalizability of the conclusions specifically to oral cancer screening.

Future perspective

In shaping the future landscape of oral cancer screening, it is imperative to prioritize research initiatives and the advancement of innovative screening technologies. Emphasizing research priorities will deepen our understanding of the disease, enabling the identification of novel biomarkers, risk factors, and therapeutic targets. The development of cutting-edge screening technologies, incorporating elements of AI, molecular diagnostics, and non-invasive imaging modalities, holds significant promise. Integrating these advancements can enhance early detection accuracy, improve screening accessibility, and streamline diagnostic processes. Additionally, fostering collaborative efforts among researchers, healthcare professionals, and technology developers will be instrumental in translating scientific discoveries into practical and impactful tools for effective oral cancer screening in the future.

Conclusions

Oral cancer poses a significant public health challenge, with a rising incidence among young people. Risk factors for oral cancer include tobacco or bidi smoking, betel quid chewing, heavy alcohol consumption, micronutrient deficiency, and HPV infection. Prevention and early detection through primary prevention strategies, screening methods, and awareness programs are crucial in reducing the incidence and mortality associated with oral cancer. Different screening techniques, such as visual examination, toluidine blue staining, autofluorescence imaging, and salivary biomarkers, can aid in the early detection of oral cancer. The integration of AI into screening programs may improve the efficiency and accuracy of oral cancer diagnostics. Continued research, technological advancements, and collaborative efforts are vital for improving screening accuracy, expanding access to underserved populations, and ultimately reducing the burden of oral cancer through early detection and intervention.

Acknowledgments

None.

Funding

The authors received no funding for this study.

Conflict of interest

The author has no conflict of interest to declare.

Author contributions

AKJ is the sole author of the manuscript.

References

- [1] Sarode G, Maniyar N, Sarode SC, Jafer M, Patil S, Awan KH. Epidemiologic aspects of oral cancer. *Dis Mon* 2020;66(12):100988. doi:10.1016/j.disamonth.2020.100988, PMID:32605720.
- [2] Ketabat F, Pundir M, Mohabatpour F, Lobanova L, Koutsopoulos S, Hadjiiski L, *et al.* Controlled Drug Delivery Systems for Oral Cancer Treatment-Current Status and Future Perspectives. *Pharmaceutics* 2019; 11(7):302. doi:10.3390/pharmaceutics11070302, PMID:31262096.

- [3] Saka-Herrán C, Jané-Salas E, Mari-Roig A, Estrugo-Devesa A, López-López J. Time-to-Treatment in Oral Cancer: Causes and Implications for Survival. *Cancers (Basel)* 2021;13(6):1321. doi:10.3390/cancers13061321, PMID:33809427.
- [4] Abati S, Bramati C, Bondi S, Lissoni A, Trimarchi M. Oral Cancer and Precancer: A Narrative Review on the Relevance of Early Diagnosis. *Int J Environ Res Public Health* 2020;17(24):9160. doi:10.3390/ijerph17249160, PMID:33302498.
- [5] Garcia Dias da Conceição M, Cláudia Figueiró A, Lucia Luiza V. Non-Invasive Methods for Early Diagnosis of Oral Cancer. In: Sridharan G, Sukumaran A, Eddin Omar Al Ostwani A (eds). *Oral Diseases*. London: IntechOpen; 2020. doi:10.5772/intechopen.89280.
- [6] Wang S, Yang M, Li R, Bai J. Current advances in noninvasive methods for the diagnosis of oral squamous cell carcinoma: a review. *Eur J Med Res* 2023;28(1):53. doi:10.1186/s40001-022-00916-4, PMID:36707844.
- [7] Parak U, Lopes Carvalho A, Roitberg F, Mandrik O. Effectiveness of screening for oral cancer and oral potentially malignant disorders (OPMD): A systematic review. *Prev Med Rep* 2022;30:101987. doi:10.1016/j.pmedr.2022.101987, PMID:36189128.
- [8] Conway DI, Stockton DL, Warnakulasuriya KA, Ogden G, Macpherson LM. Incidence of oral and oropharyngeal cancer in United Kingdom (1990-1999) — recent trends and regional variation. *Oral Oncol* 2006;42(6):586–592. doi:10.1016/j.oraloncology.2005.10.018, PMID:16469526.
- [9] Conway DI, Purkayastha M, Chestnutt IG. The changing epidemiology of oral cancer: definitions, trends, and risk factors. *Br Dent J* 2018;225(9):867–873. doi:10.1038/sj.bdj.2018.922, PMID:30412558.
- [10] Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA Cancer J Clin* 2021;71(3):209–249. doi:10.3322/caac.21660, PMID:33538338.
- [11] Wahi PN. The epidemiology of oral and oropharyngeal cancer. A report of the study in Mainpuri district, Uttar Pradesh, India. *Bull World Health Organ* 1968;38(4):495–521. PMID:5302449.
- [12] Borse V, Konwar AN, Buragohain P. Oral cancer diagnosis and perspectives in India. *Sens Int* 2020;1:100046. doi:10.1016/j.sintl.2020.100046, PMID:34766046.
- [13] Warnakulasuriya S. Global epidemiology of oral and oropharyngeal cancer. *Oral Oncol* 2009;45(4-5):309–316. doi:10.1016/j.oraloncology.2008.06.002, PMID:18804401.
- [14] Byakodi R, Byakodi S, Hiremath S, Byakodi J, Adaki S, Marathe K, et al. Oral cancer in India: an epidemiologic and clinical review. *J Community Health* 2012;37(2):316–319. doi:10.1007/s10900-011-9447-6, PMID:21786206.
- [15] Siegel RL, Miller KD, Wagle NS, Jemal A. Cancer statistics, 2023. *CA Cancer J Clin* 2023;73(1):17–48. doi:10.3322/caac.21763, PMID:36633525.
- [16] National Cancer Institute. SEER Cancer Stat Facts: Oral Cavity and Pharynx Cancer. Bethesda. Available from: <https://seer.cancer.gov/statfacts/html/oralcav.html>. Accessed September, 2023.
- [17] Bagan J, Sarrion G, Jimenez Y. Oral cancer: clinical features. *Oral Oncol* 2010;46(6):414–417. doi:10.1016/j.oraloncology.2010.03.009, PMID:20400366.
- [18] Scully C, Bagan J. Oral squamous cell carcinoma: overview of current understanding of aetiopathogenesis and clinical implications. *Oral Dis* 2009;15(6):388–399. doi:10.1111/j.1601-0825.2009.01563.x, PMID:19371401.
- [19] Petti S. Lifestyle risk factors for oral cancer. *Oral Oncol* 2009;45(4-5):340–350. doi:10.1016/j.oraloncology.2008.05.018, PMID:18674956.
- [20] Lissoni A, Agliardi E, Peri A, Marchioni R, Abati S. Oral microbiome and mucosal trauma as risk factors for oral cancer: beyond alcohol and tobacco. A literature review. *J Biol Regul Homeost Agents* 2020;34(6 Suppl. 3):()11–18. PMID:33386052.
- [21] Rivera C. Essentials of oral cancer. *Int J Clin Exp Pathol* 2015;8(9):11884–11894. PMID:26617944.
- [22] Sarode GS, Batra A, Sarode SC, Yerawadekar S, Patil S. Oral Cancer-related Inherited Cancer Syndromes: A Comprehensive Review. *J Contemp Dent Pract* 2016;17(6):504–510. doi:10.5005/jp-journals-10024-1880, PMID:27484606.
- [23] Zain RB. Cultural and dietary risk factors of oral cancer and precancer—a brief overview. *Oral Oncol* 2001;37(3):205–210. doi:10.1016/s1368-8375(00)00133-0, PMID:11287272.
- [24] Joseph BK. Oral cancer: prevention and detection. *Med Princ Pract* 2002;11(Suppl 1):32–35. doi:10.1159/000057776, PMID:12123114.
- [25] Speight PM, Epstein J, Kujan O, Lingen MW, Nagao T, Ranganathan K, et al. Screening for oral cancer—a perspective from the Global Oral Cancer Forum. *Oral Surg Oral Med Oral Pathol Oral Radiol* 2017;123(6):680–687. doi:10.1016/j.oooo.2016.08.021, PMID:27727113.
- [26] Warnakulasuriya S, Kerr AR. Oral Cancer Screening: Past, Present, and Future. *J Dent Res* 2021;100(12):1313–1320. doi:10.1177/00220345211014795, PMID:34036828.
- [27] Brocklehurst P, Kujan O, O'Malley LA, Ogden G, Shepherd S, Glenny AM. Screening programmes for the early detection and prevention of oral cancer. *Cochrane Database Syst Rev* 2013;2013(11):CD004150. doi:10.1002/14651858.CD004150.pub4, PMID:24254989.
- [28] Li YN, Lu R, Zhang J, Zhou G. Inter-and intra-observer agreement on the judgment of toluidine blue staining for screening of oral potentially malignant disorders and oral cancer. *Clin Oral Investig* 2019;23(4):1709–1714. doi:10.1007/s00784-018-2595-7, PMID:30155573.
- [29] Zhang L, Williams M, Poh CF, Laronde D, Epstein JB, Durham S, et al. Toluidine blue staining identifies high-risk primary oral premalignant lesions with poor outcome. *Cancer Res* 2005;65(17):8017–8021. doi:10.1158/0008-5472.CAN-04-3153, PMID:16140975.
- [30] Awan KH, Patil S. Efficacy of Autofluorescence Imaging as an Adjunctive Technique for Examination and Detection of Oral Potentially Malignant Disorders: A Systematic Review. *J Contemp Dent Pract* 2015;16(9):744–749. doi:10.5005/jp-journals-10024-1751, PMID:26522601.
- [31] Walsh T, Macey R, Kerr AR, Lingen MW, Ogden GR, Warnakulasuriya S. Diagnostic tests for oral cancer and potentially malignant disorders in patients presenting with clinically evident lesions. *Cochrane Database Syst Rev* 2021;7(7):CD010276. doi:10.1002/14651858.CD010276.pub3, PMID:34282854.
- [32] Kim DH, Kim SW, Hwang SH. Efficacy of optical coherence tomography in the diagnosing of oral cancerous lesion: systematic review and meta-analysis. *Head Neck* 2023;45(2):473–481. doi:10.1002/hed.27232, PMID:36305811.
- [33] Chakraborty D, Natarajan C, Mukherjee A. Advances in oral cancer detection. *Adv Clin Chem* 2019;91:181–200. doi:10.1016/bs.acc.2019.03.006, PMID:31331489.
- [34] Wong DT. Salivaomics. *J Am Dent Assoc* 2012;143(10 Suppl):19S–24S. doi:10.14219/jada.archive.2012.0339, PMID:23034834.
- [35] Kaur J, Jacobs R, Huang Y, Salvo N, Politis C. Salivary biomarkers for oral cancer and pre-cancer screening: a review. *Clin Oral Investig* 2018;22(2):633–640. doi:10.1007/s00784-018-2337-x, PMID:29344805.
- [36] Candotto V, Lauritano D, Nardone M, Baggi L, Arcuri C, Gatto R, et al. HPV infection in the oral cavity: epidemiology, clinical manifestations and relationship with oral cancer. *Oral Implantol (Rome)* 2017;10(3):209–220. doi:10.11138/orl/2017.10.3.209, PMID:29285322.
- [37] Bettampadi D, Sirak BA, Fulp WJ, Abrahamsen M, Villa LL, Lazcano-Ponce E, et al. Oral HPV prevalence assessment by Linear Array vs. SPF10 PCR-DEIA-LiPA25 system in the HPV Infection in Men (HIM) study. *Papillomavirus Res* 2020;9:100199. doi:10.1016/j.pvr.2020.100199, PMID:32464335.
- [38] Tang KD, Vasani S, Menezes L, Taheri T, Walsh LJ, Hughes BGM, et al. Oral HPV16 DNA as a screening tool to detect early oropharyngeal squamous cell carcinoma. *Cancer Sci* 2020;111(10):3854–3861. doi:10.1111/cas.14585, PMID:32713038.
- [39] Gipson BJ, Robbins HA, Fakhry C, D'Souza G. Sensitivity and specificity of oral HPV detection for HPV-positive head and neck cancer. *Oral Oncol* 2018;77:52–56. doi:10.1016/j.oraloncology.2017.12.008, PMID:29362127.
- [40] Ilhan B, Lin K, Guneri P, Wilder-Smith P. Improving Oral Cancer Outcomes with Imaging and Artificial Intelligence. *J Dent Res* 2020;99(3):241–248. doi:10.1177/0022034520902128, PMID:32077795.
- [41] Birur N P, Song B, Sunny SP, G K, Mendonca P, Mukhia N, et al. Field validation of deep learning based Point-of-Care device for

- early detection of oral malignant and potentially malignant disorders. *Sci Rep* 2022;12(1):14283. doi:10.1038/s41598-022-18249-x, PMID:35995987.
- [42] Hegde S, Ajila V, Zhu W, Zeng C. Artificial intelligence in early diagnosis and prevention of oral cancer. *Asia Pac J Oncol Nurs* 2022;9(12):100133. doi:10.1016/j.apjon.2022.100133, PMID:36389623.
- [43] Morikawa T, Shibahara T, Takano M, Iwamoto M, Takaki T, Kasahara K, *et al.* Countermeasure and opportunistic screening systems for oral cancer. *Oral Oncol* 2021;112:105047. doi:10.1016/j.oraloncology.2020.105047, PMID:33129059.
- [44] Mohan P, Richardson A, Potter JD, Coope P, Paterson M. Opportunistic Screening of Oral Potentially Malignant Disorders: A Public Health Need for India. *JCO Glob Oncol* 2020;6:688–696. doi:10.1200/JGO.19.00350, PMID:32364799.
- [45] Kaur R, Kant S, Mathur VP, Lohia A. Feasibility of opportunistic screening for oral cancers in a dental outpatient department of a secondary care hospital in Northern India. *J Family Med Prim Care* 2020;9(2):909–914. doi:10.4103/jfmpc.jfmpc_999_19, PMID:32318444.
- [46] Speight PM, Palmer S, Moles DR, Downer MC, Smith DH, Henriksson M, *et al.* The cost-effectiveness of screening for oral cancer in primary care. *Health Technol Assess* 2006;10(14):1–144, iii–iv. doi:10.3310/hta10140, PMID:16707071.
- [47] Lee YA, Al-Temimi M, Ying J, Muscat J, Olshan AF, Zavallos JP, *et al.* Risk Prediction Models for Head and Neck Cancer in the US Population From the INHANCE Consortium. *Am J Epidemiol* 2020;189(4):330–342. doi:10.1093/aje/kwz259, PMID:31781743.
- [48] Amarasinghe HK, Johnson NW, Laloo R, Kumaraarachchi M, Warnakulasuriya S. Derivation and validation of a risk-factor model for detection of oral potentially malignant disorders in populations with high prevalence. *Br J Cancer* 2010;103(3):303–309. doi:10.1038/sj.bjc.6605778, PMID:20628386.
- [49] Tota JE, Gillison ML, Katki HA, Kahle L, Pickard RK, Xiao W, *et al.* Development and validation of an individualized risk prediction model for oropharynx cancer in the US population. *Cancer* 2019;125(24):4407–4416. doi:10.1002/cncr.32412, PMID:31454434.