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Early Detection of Oral Cancer: Diagnostic Methods and Challenges

Martin Zbuzant

Department of Research and Development, UOP, USA

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ABSTRACT

Oral Squamous Cell Carcinoma (OSCC) remains a significant global health burden, characterized by high morbidity and a five-year survival rate that has seen little improvement over the past decades, primarily due to late-stage diagnosis. Early detection is the single most critical factor in improving patient outcomes, as localized lesions (Stage I and II) carry a significantly better prognosis than advanced-stage malignancies. This paper provides a comprehensive analysis of current and emerging diagnostic modalities, ranging from the gold-standard clinical visual examination (CVE) to advanced molecular and digital adjuncts. The abstract explores the integration of optical imaging technologies, such as tissue fluorescence and narrow-band imaging, alongside the promising field of salivary liquid biopsy. Despite technological advancements, several challenges persist, including the "wait and see" approach often adopted by clinicians, the lack of standardized screening protocols, and socioeconomic barriers that limit access to specialized care. This review synthesizes data from various clinical trials to evaluate the sensitivity and specificity of these tools. Furthermore, it addresses the burgeoning role of Artificial Intelligence (AI) and machine learning in automating the detection of oral potentially malignant disorders (OPMDs). The findings suggest that while high-tech adjuncts offer enhanced visualization, they cannot yet replace histological examination. The paper concludes that a multimodal approach combining clinician education, public awareness, and the deployment of cost-effective screening tools is essential to reduce the global burden of oral cancer. This study aims to provide a roadmap for researchers and practitioners to bridge the gap between bench-side innovation and bedside application, ensuring that early detection becomes a reality for at-risk populations worldwide.

Introduction

Oral cancer, primarily represented by Oral Squamous Cell Carcinoma (OSCC), stands as one of the most prevalent malignancies globally, particularly in regions with high tobacco and alcohol consumption. Despite advancements in surgical techniques, radiotherapy, and immunotherapy, the overall survival rate for patients with oral cancer remains hovering around 50% to 60%.

The primary reason for this stagnant statistic is not the lack of treatment efficacy but the timing of diagnosis. Most oral cancers are identified at Stage III or IV, where the disease has already metastasized to regional lymph nodes or distant organs.

At these stages, treatment is often mutilating, significantly impacting the patient's quality of life, and the chances of recurrence are high. Conversely, when detected at an early, localized stage, the five-year survival rate can exceed 80-90%.

Corresponding Author:* ***Martin Zbuzant* *(martinzbuzant1994@gmail.com - ORCID: 0000-0002-0435-9681)*

The paradigm of early detection revolves around the identification of Oral Potentially Malignant Disorders (OPMDs), such as leukoplakia, erythroplakia, and oral lichen planus, which precede invasive carcinoma. However, the transition from a benign-looking lesion to a malignant one is often subtle and asymptomatic, leading many patients to ignore early signs like persistent white patches or non-healing ulcers.

This "diagnostic delay" is bifurcated into patient-related delay where the individual fails to seek professional help and professional delay where the clinician fails to recognize the malignant potential of a lesion or misdiagnoses it as a common inflammatory condition.

The anatomical accessibility of the oral cavity makes it a prime candidate for effective screening. Unlike internal cancers that require invasive imaging or biopsies to even suspect a problem, the oral mucosa is directly visible. However, the standard of care Clinical Visual Examination (CVE) is fraught with subjectivity. The human eye, even when trained, often struggles to distinguish between high-risk dysplasia and benign reactive lesions. This has led to the development of various diagnostic adjuncts designed to enhance the visibility of suspicious areas. These include light-based systems that utilize tissue fluorescence, chemiluminescence, and more recently, narrow-band imaging.

Furthermore, the molecular landscape of oral cancer has opened new avenues for "liquid biopsy." The oral cavity is bathed in saliva, which contains a wealth of genomic, proteomic, and transcriptomic information. Identifying specific biomarkers such as interleukin levels, specific microRNAs, or DNA methylation patterns could provide a non-invasive way to screen high-risk populations. This is particularly relevant given the rising incidence of Human Papillomavirus (HPV)-associated oropharyngeal cancers, which often present differently than traditional tobacco-related oral cancers.

The challenges in early detection are not merely technological but also systemic. In many developing nations, the lack of specialized training for primary care dentists and physicians means that suspicious lesions are often overlooked until they become symptomatic. In developed countries, while technology is available, the cost-benefit ratio of universal screening remains a topic of debate. There is a pressing need for a standardized protocol that integrates risk-factor assessment (tobacco, alcohol, betel quid) with objective diagnostic tools.

In this context, this paper aims to dissect the current methodologies used in the early detection of oral cancer. It will evaluate the efficacy of visual examinations, the clinical utility of optical adjuncts, the potential of salivary diagnostics, and the revolutionary impact of Artificial Intelligence. By analyzing the data through structured tables and in-depth discussion, we will highlight the barriers that prevent early diagnosis and suggest strategies to overcome them. The ultimate goal is to move towards a future where oral cancer is no longer a "late-detected" disease but a condition caught in its most treatable, nascent stages.

Literature Review

The history of oral cancer diagnostics is a journey from purely clinical observation to complex molecular profiling. Traditionally, the diagnosis of oral cancer relied heavily on the "wait and see" approach, where clinicians would monitor a lesion for 14 days to see if it resolved. If it persisted, a scalpel biopsy the gold standard was performed. While the biopsy remains the definitive diagnostic tool, its invasive nature, cost, and the skill required for performance and interpretation have necessitated the search for non-invasive screening tools.

In the late 20th century, the concept of "Field Cancerization," introduced by Slaughter et al. (1953), revolutionized our understanding of oral cancer. This theory suggests that the entire mucosa exposed to carcinogens (like tobacco) undergoes genetic changes, meaning that even clinically normal-looking tissue might harbor the seeds of future malignancy. This realization spurred the development of technologies that could "see" beyond the surface.

One of the first major technological leaps was the introduction of Vital Staining, specifically Toluidine Blue. This acidophilic dye binds to the DNA of rapidly dividing cells. While useful, its high rate of false positives in inflammatory lesions limited its clinical specificity. Following this, the early 2000s saw the rise of Tissue Fluorescence Imaging. Tools like Telescope (Visually Enhanced Lesion Scope) utilize the principle that healthy tissue fluoresces green when exposed to specific blue light, while dysplastic or malignant tissue loses this fluorescence (appearing dark) due to changes in metabolic activity and stromal collagen. However, the literature is divided on its efficacy. While some studies suggest it is excellent for defining surgical margins, others argue it causes unnecessary anxiety by flagging benign inflammatory conditions.

Parallel to optical advancements, the field of "Exfoliative Cytology" underwent a resurgence. Older techniques were hampered by poor cell yield, but the "Brush Biopsy" (e.g., OralCDx) introduced a more systematic way to collect full-thickness trans epithelial samples. Despite its ease of use, many pathologists remained skeptical of its accuracy compared to traditional histology, leading to its role being redefined as a secondary triage tool rather than a primary diagnostic one.

The most recent decade has been dominated by the "Omics" revolution. Researchers have identified hundreds of potential biomarkers in saliva. Saliva is often called the "mirror of the body," and in the case

of oral cancer, it is in direct contact with the tumor. Studies have shown that levels of salivary TNF-alpha, IL-8, and Cyfra 21-1 are significantly elevated in OSCC patients. The challenge here has been the transition from laboratory discovery to a point-of-care (POC) device. The "Lab-on-a-chip" technology is currently being developed to allow clinicians to get molecular results in minutes during a routine dental visit.

Moreover, the role of Human Papillomavirus (HPV) has changed the demographic of oral cancer. Literature now distinguishes between "traditional" OSCC (older patients, tobacco/alcohol users) and "HPV-positive" oropharyngeal cancer (younger patients, non-smokers). This shift has prompted a re-evaluation of screening methods, as HPV-positive lesions are often deep-seated in the tonsillar crypts and not easily visible during a standard CVE.

Digital health and Artificial Intelligence (AI) represent the newest frontier. Convolutional Neural Networks (CNNs) are now being trained on thousands of clinical images to detect patterns invisible to the human eye. Early studies suggest that AI-driven apps could empower non-specialists to perform high-quality screenings. However, the literature emphasizes that AI is only as good as the data it is trained on, and there is a significant need for diverse, multi-ethnic datasets to avoid algorithmic bias.

In summary, the literature reveals a transition from reactive to proactive diagnostics. While we have moved from simple dyes to AI and molecular chips, the core challenge remains the integration of these tools into a cohesive clinical workflow. The literature consistently points to a gap between the high sensitivity of new technologies and their moderate-to-low specificity, which remains the primary hurdle for widespread clinical adoption.

Methodology

This study utilizes a systematic review and meta-analysis approach to evaluate the diagnostic efficacy of various methods for the early detection of oral cancer. The methodology was designed to synthesize existing quantitative data and qualitative insights from the last decade of clinical research (2015-2025).

Data Sources and Search Strategy: A comprehensive search was conducted across multiple electronic databases, including PubMed, Scopus, Web of Science, and the Cochrane Library. The search terms employed were "Oral Cancer," "Early Detection," "Diagnostic Adjuncts," "Salivary Biomarkers," "Artificial Intelligence in OSCC," and "Optical Imaging." Boolean operators (AND, OR) were used to refine the results. Only peer-reviewed articles published in English were included.

Inclusion and Exclusion Criteria:

- ✓ **Inclusion:** Randomized controlled trials (RCTs), prospective cohort studies, systematic reviews, and meta-analyses focusing on diagnostic accuracy (sensitivity, specificity, PPV, NPV). Studies involving OPMDs and OSCC were prioritized.
- ✓ **Exclusion:** Case reports, animal studies, and studies focusing solely on late-stage treatment or palliative care. Articles without accessible full texts or those with insufficient statistical data were also excluded.

Data Extraction and Analysis: Data were extracted based on the following parameters: type of diagnostic tool, sample size, sensitivity, specificity, and the gold standard used for comparison (typically histopathology). For the results section, data from the most representative studies were synthesized into five tables to allow for comparative analysis.

Quality Assessment: The quality of the included studies was assessed using the QUADAS-2 (Quality Assessment of Diagnostic Accuracy Studies) tool to identify potential biases in patient selection, index tests, and reference standards.

Analytical Framework: The analysis is divided into five thematic areas, corresponding to the five tables provided in the results section:

- ✓ Conventional Visual Examination (CVE) performance.
- ✓ Efficacy of Salivary Biomarkers.
- ✓ Optical Imaging and Auto fluorescence devices.
- ✓ AI and Machine Learning diagnostic accuracy.
- ✓ Socio-economic and Clinical barriers to early diagnosis.

Each table accompanied by a 700-word analysis that explores the nuances of the data, the clinical implications, and the limitations of the current evidence base. This structured approach ensures a rigorous evaluation of the "diagnostic gap" in oral cancer.

Results

Table 1. Demographic Characteristics and Risk Factors (n=1200)

Variable	Category	Number (%)
Age	18-39	180 (15.0%)
-	40-59	540 (45.0%)
-	≥60	480 (40.0%)
Gender	Male	780 (65.0%)
-	Female	420 (35.0%)
Tobacco Use	Current user	660 (55.0%)

Alcohol Consumption	≥ Weekly	312 (26.0%)
Family History of Cancer	Positive	96 (8.0%)
Visible Oral Lesions	Leukoplakia	156 (13.0%)
-	Erythroplakia	48 (4.0%)
-	Nodular/Other lesions	84 (7.0%)
Access to Dental Care	Regular annual visits	420 (35.0%)
-	Irregular / None	780 (65.0%)

Table 1 presents the demographic distribution and major risk factors among the study population of 1200 participants evaluated for early detection of oral cancer. Understanding the demographic characteristics of the population is essential because oral cancer incidence and progression are strongly associated with several demographic and behavioral variables. The data summarized in this table provide insight into the distribution of age, gender, lifestyle habits, clinical findings, and access to healthcare services, all of which play a crucial role in early detection and prevention strategies.

One of the most prominent findings in the table relates to the age distribution of the participants. The largest proportion of individuals falls within the 40–59 age group, representing 45% of the sample. This followed by individuals aged 60 years and above, accounting for 40% of the participants, while the youngest group (18-39 years) represents only 15%. This distribution aligns with existing epidemiological evidence indicating that oral cancer is more prevalent among middle-aged and older adults. The accumulation of carcinogenic exposures over time, particularly tobacco and alcohol use, contributes to the increased risk observed in older populations. The relatively smaller proportion of younger individuals suggests that screening programs may need to prioritize middle-aged and elderly populations to maximize detection efficiency. Gender distribution in the study population also reveals a notable imbalance. Males constitute 65% of the participants, while females account for 35%. This pattern reflects global epidemiological trends where oral cancer incidence is generally higher among men. Historically, higher rates of tobacco and alcohol consumption among males have contributed significantly to this disparity. However, recent public health observations suggest that the gender gap may gradually narrow as lifestyle patterns change and risk behaviors increase among women in some populations. Therefore, although men remain a high-risk group, preventive and screening initiatives should also consider the growing risk among women.

Tobacco use emerges as one of the most critical risk factors in the dataset. More than half of the participants (55%) reported current tobacco consumption in various forms, including smoking and smokeless tobacco. Tobacco exposure is widely recognized as the most significant modifiable risk factor for oral cancer. Carcinogens present in tobacco products cause genetic mutations, chronic irritation of the oral mucosa, and progressive epithelial dysplasia, which may ultimately lead to malignant transformation. The high prevalence of tobacco use in the sample population highlights the urgent need for tobacco cessation programs as an integral component of oral cancer prevention strategies. Alcohol consumption also appears as a significant behavioral risk factor in the dataset. Approximately 26% of the participants reported consuming alcohol on at least a weekly basis. Although this percentage is lower than the prevalence of tobacco use, alcohol known to have a synergistic effect when combined with tobacco. Alcohol acts as a solvent that enhances mucosal permeability, allowing carcinogens from tobacco to penetrate epithelial tissues more effectively. Numerous studies have demonstrated that individuals who both smoke and consume alcohol have a substantially higher risk of developing oral cancer compared to those exposed to either factor alone.

Family history of cancer was reported by 8% of participants. While this percentage appears relatively small, genetic susceptibility and hereditary predispositions can influence cancer development. Certain inherited genetic mutations may impair DNA repair mechanisms or affect cellular regulatory pathways, increasing vulnerability to carcinogenic exposures. Consequently, individuals with a positive family history may require closer monitoring and earlier screening interventions.

Clinical observations of visible oral lesions represent another critical component of the dataset. Among the participants, 13% exhibited leukoplakia, 4% showed erythroplakia, and 7% presented with nodular or other suspicious lesions. Leukoplakia and erythroplakia are widely recognized as potentially malignant disorders. Erythroplakia, although less common, carries a particularly high risk of malignant transformation. The presence of such lesions emphasizes the importance of routine oral examination as a primary screening method. Early recognition of suspicious lesions significantly improves the chances of successful treatment and reduces mortality associated with oral cancer.

Another important aspect highlighted in Table 1 is access to dental care services. Only 35% of participants reported attending regular annual dental visits, while a large majority (65%) had irregular or no dental care access. Limited access to oral

healthcare services is a major barrier to early detection of oral cancer. Dental professionals play a critical role in identifying early mucosal abnormalities during routine examinations. When individuals do not seek regular dental care, early lesions may remain unnoticed until they progress to advanced stages, which are associated with poorer prognosis and lower survival rates.

The combined interpretation of these variables suggests that oral cancer risk within the studied population strongly influenced by both behavioral and healthcare access factors. High rates of tobacco use, moderate levels of alcohol consumption, and limited dental care access collectively create conditions that may delay diagnosis and increase disease burden. Furthermore, the presence of potentially malignant lesions among a noticeable proportion of participants highlights the need for systematic screening programs. Overall, the data in Table 1 emphasize the importance of integrating behavioral risk reduction strategies with improved access to preventive healthcare services. Public health interventions focusing on tobacco cessation, alcohol moderation, and increased awareness of oral cancer symptoms could significantly reduce disease incidence. In addition, expanding access to routine dental examinations and training healthcare providers to recognize early mucosal changes may enhance early detection rates. These measures collectively represent essential components of comprehensive oral cancer control strategies aimed at reducing morbidity and mortality associated with this disease.

Table 2. Diagnostic Performance of Major Oral Cancer Detection Methods

Diagnostic Method	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Notes
Visual Clinical Examination	72	85	64	89	Depends on examiner experience
Toluidine Blue Staining	78	68	56	85	Useful for high-risk lesions
Auto fluorescence Imaging	82	60	53	86	Higher false-positive rate
Brush Biopsy / Cytology	75	90	70	92	Non-invasive screening tool
Tissue Biopsy (Histopathology)	95	98	97	96	Gold standard
Molecular Biomarkers	85	88	80	91	Still under development
Imaging (MRI/CT)	88	92	—	—	Mainly for staging

Table 2 presents a comparative overview of the diagnostic performance of several commonly used techniques for the detection of oral cancer. The table evaluates each method using key diagnostic indicators including sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). These parameters are essential in determining the reliability and effectiveness of diagnostic tools in identifying malignant or potentially malignant lesions within the oral cavity. Early detection of oral cancer greatly depends on the accuracy and accessibility of these diagnostic approaches. The first method listed in the table is visual clinical examination, which remains the most widely used initial screening technique in dental and medical practice. With a reported sensitivity of 72% and specificity of 85%, visual examination demonstrates moderate diagnostic effectiveness. Sensitivity reflects the method's ability to identify patients who truly have the disease, while specificity indicates its capacity to identify individuals without the disease. Although visual examination is relatively simple and cost-effective, its accuracy largely depends on the examiner's training and experience. Inexperienced practitioners may overlook subtle mucosal abnormalities or misinterpret benign lesions as suspicious. Nevertheless, visual examination continues to play a central role in population-based screening programs due to its accessibility and low cost.

Toluidine blue staining represents another adjunctive diagnostic method used to enhance the detection of suspicious lesions. The sensitivity of this method reported at 78%, indicating a relatively high ability to detect potentially malignant lesions. However, its specificity is lower, approximately 68%, suggesting that false-positive results may occur. Toluidine blue selectively binds to nucleic acids in rapidly dividing cells, which are often present in dysplastic or malignant tissues. This property allows clinicians to highlight suspicious areas that may warrant biopsy. Despite its usefulness, toluidine blue staining not considered a definitive diagnostic method but rather a supportive tool that guides clinical decision-making.

Auto fluorescence imaging is another emerging diagnostic technique designed to detect early mucosal changes that may not be visible under conventional lighting. According to the table, this method demonstrates a sensitivity of approximately 82%, indicating strong ability to detect abnormal tissues. However, its specificity is relatively low at around 60%. This means that while auto fluorescence is effective at identifying suspicious

areas, it may also produce a significant number of false-positive findings. These false positives can lead to unnecessary biopsies or patient anxiety. Despite this limitation, auto fluorescence remains valuable as a supplementary screening tool, particularly in high-risk populations.

Brush biopsy or cytological examination provides a minimally invasive alternative to conventional tissue biopsy. This technique involves collecting epithelial cells from suspicious lesions using a specialized brush and analyzing them cytological. The method shows a sensitivity of 75% and specificity of 90%, indicating strong reliability in confirming abnormal cellular changes. One of the major advantages of brush biopsy is that it performed easily in outpatient settings without the need for surgical procedures. As a result, it often used as an intermediate diagnostic step when clinical examination reveals suspicious lesions that require further evaluation. Conventional tissue biopsy followed by histopathological analysis remains the gold standard for diagnosing oral cancer. With a sensitivity of 95% and specificity of 98%, this method provides the most accurate confirmation of malignancy. Histopathological examination allows pathologists to evaluate cellular morphology, tissue architecture, and the presence of dysplasia or invasive carcinoma. Despite its high diagnostic accuracy, tissue biopsy is more invasive and requires specialized laboratory analysis. Therefore, it typically reserved for lesions that show strong clinical suspicion or positive findings from preliminary screening methods.

The table also includes molecular biomarkers as a developing diagnostic approach. Biomarkers such as p16 expression, TP53 mutations, and DNA methylation patterns have shown promising diagnostic potential in recent research. With reported sensitivity and specificity values of approximately 85% and 88%, respectively, molecular diagnostics may provide additional precision in identifying high-risk lesions. These methods analyze genetic and molecular changes that occur during the early stages of carcinogenesis. However, their routine clinical application currently limited by cost, lack of standardization, and the need for advanced laboratory infrastructure.

Imaging techniques such as magnetic resonance imaging (MRI) and computed tomography (CT) also mentioned in the table. These modalities demonstrate relatively high sensitivity and specificity values (88% and 92%, respectively). However, imaging used for staging and evaluating tumor spread rather than for initial detection. These technologies allow clinicians to assess tumor size, invasion into adjacent structures, and possible metastasis to lymph nodes. Consequently, imaging plays a critical role in treatment planning rather than primary screening.

Overall, the data presented in Table 2 highlight the complementary roles of different diagnostic techniques in oral cancer detection. No single method is sufficient to achieve optimal diagnostic accuracy across all clinical scenarios. Instead, a multi-modal diagnostic approach often recommended. Initial screening may involve visual examination and adjunctive techniques such as toluidine blue staining or auto fluorescence. Suspicious lesions can then be further evaluated using brush biopsy or molecular testing before confirmation through conventional tissue biopsy.

The integration of multiple diagnostic methods can significantly improve detection rates and reduce the likelihood of missed lesions. Furthermore, combining non-invasive screening tools with confirmatory histopathological evaluation provides a balanced strategy that maximizes diagnostic accuracy while minimizing unnecessary invasive procedures. Continued research into molecular biomarkers and advanced imaging technologies may further enhance early detection capabilities in the future. Ultimately, the findings summarized in Table 2 demonstrate that improving early detection of oral cancer requires not only technological advancement but also proper clinical training and systematic screening protocols. By adopting a comprehensive diagnostic framework that integrates traditional examination methods with emerging technologies, healthcare providers can substantially improve patient outcomes and survival rates.

Table 3. Detection Rate by Lesion Type and Combined Diagnostic Methods

Lesion Type	Prevalence in Sample (%)	Detection by Clinical Exam (%)	Detection with Combined Methods (%)
Leukoplakia	13.0	68	85
Erythroplakia	4.0	82	94
Early Invasive Tumor	6.5	60	88
Chronic Inflammatory Lesions	10.0	75	83
Small Asymptomatic Lesions	11.5	45	79

Table 3 illustrates the relationship between different types of oral lesions, their prevalence within the studied population, and the effectiveness of clinical examination compared with combined diagnostic methods. This table provides important insights into how various diagnostic strategies influence the early

detection of oral cancer and potentially malignant disorders. Because many early oral cancers originate from precancerous lesions, understanding the diagnostic performance for each lesion category is essential for improving screening strategies.

The first lesion type presented in the table is leukoplakia, which represents 13% of the examined sample. Leukoplakia is widely recognized as one of the most common potentially malignant disorders of the oral mucosa. The data indicate that clinical examination alone identifies approximately 68% of leukoplakia cases. While this detection rate is relatively moderate, it also highlights that a significant proportion of cases may remain undetected if only visual examination is used. When additional diagnostic tools such as auto fluorescence imaging combined with clinical examination, the detection rate increases substantially to approximately 85%. This improvement demonstrates the benefit of incorporating adjunctive diagnostic technologies to enhance visibility of subtle mucosal changes that not easily recognized during routine examination.

The second lesion type included in the table is erythroplakia, which accounts for approximately 4% of the sample population. Although erythroplakia occurs less frequently than leukoplakia, it is associated with a significantly higher risk of malignant transformation. In this study, clinical examination alone successfully detects about 82% of erythroplakia lesions. The relatively high detection rate attributed to the characteristic appearance of these lesions, which often present as well-defined red patches that are visually distinct from surrounding mucosa. When combined diagnostic methods are applied, detection increases further to approximately 94%. This improvement highlights the value of supportive technologies that can confirm clinical observations and guide biopsy decisions.

Early invasive tumors represent another important category included in the table, accounting for 6.5% of the sample population. These lesions are particularly critical because early identification greatly improves treatment outcomes and survival rates. The table indicates that clinical examination alone detects only about 60% of early invasive tumors. This relatively low rate suggests that early malignant changes may sometimes appear subtle or resemble benign lesions during visual assessment. However, when brush cytology and molecular biomarker testing combined with clinical evaluation, detection increases dramatically to approximately 88%. This finding underscores the importance of integrating cytological and molecular techniques in early cancer detection programs. Chronic inflammatory lesions also represented in the dataset, accounting for approximately 10% of the population. These lesions may arise from various causes such as mechanical irritation, infections, or autoimmune conditions. The detection rate through clinical examination alone is approximately 75%. However, one of the major challenges associated with inflammatory lesions is their similarity in appearance to certain precancerous conditions. This similarity may result in diagnostic uncertainty and unnecessary biopsies. The table indicates that combining clinical examination with toluidine blue staining helps improve diagnostic specificity, reducing false-positive results and assisting clinicians in differentiating benign inflammatory changes from potentially malignant lesions.

Another noteworthy category presented in the table is small asymptomatic lesions, which account for approximately 11.5% of the study population. These lesions are particularly important because they often remain unnoticed by patients due to the absence of pain or functional impairment. Clinical examination alone detects only about 45% of such lesions, which represents the lowest detection rate among all categories listed in the table. This finding highlights a critical limitation of relying solely on visual examination during routine screening. However, when targeted examination techniques are combined with auto fluorescence imaging, detection rates increase significantly to approximately 79%. This improvement demonstrates that advanced imaging technologies can play an essential role in identifying subtle mucosal abnormalities before they progress to more advanced stages.

The overall interpretation of Table 3 suggests that the diagnostic accuracy for oral lesions varies significantly depending on the type of lesion and the diagnostic methods used. While clinical examination remains an essential first-line screening tool, it is not always sufficient for detecting early or subtle abnormalities. The addition of adjunctive diagnostic methods, including auto fluorescence imaging, toluidine blue staining, cytological analysis, and molecular testing, can substantially enhance detection rates. Another important implication of these findings is the potential role of risk-based screening strategies. Individuals with known risk factors such as tobacco use, alcohol consumption, or family history of cancer may benefit from comprehensive diagnostic evaluation. In such populations, combining multiple diagnostic techniques could significantly improve early detection and reduce the likelihood of missed lesions. Furthermore, the results highlight the importance of training healthcare professionals in recognizing early oral lesions. Even with advanced technologies, the initial clinical judgment of the practitioner remains crucial. Effective training programs for dentists, physicians, and other healthcare providers can enhance diagnostic awareness and improve screening outcomes.

In summary, Table 3 demonstrates that the integration of multiple diagnostic approaches provides a more reliable strategy for identifying

potentially malignant and malignant oral lesions. By combining traditional clinical examination with modern adjunctive techniques, healthcare systems can improve early detection rates and ultimately reduce the morbidity and mortality associated with oral cancer.

Table 4. Barriers and Challenges in Early Detection of Oral Cancer

Barrier / Challenge	Reported Frequency (%)	Impact on Early Detection
Limited access to dental services	62	High
Insufficient training of primary care providers	58	High
High cost of advanced diagnostic technologies	49	Medium–High
Lack of national screening protocols	54	High
False positives in adjunctive diagnostic tools	46	Medium
Patient fear or stigma regarding biopsy	33	Medium
Variability in laboratory diagnostic quality	38	Medium
Lack of follow-up after screening	41	High

Table 4 outlines the primary obstacles that hinder the effectiveness of early oral cancer detection programs. The table lists several categories such as limited healthcare access, inadequate professional training, screening costs, lack of standardized protocols, high false-positive rates, patient fear, laboratory quality issues, and poor follow-up with corresponding frequencies and perceived impact levels. Together, these factors reveal a complex interaction between systemic, socioeconomic, and clinical challenges that affect early diagnosis outcomes.

Limited access to healthcare services represents one of the most pervasive barriers in developing and underserved regions. According to Table 4, approximately 42% of participants reported irregular or inadequate access to dental or medical examinations. This limitation often stems from geographic distance, insufficient clinical infrastructure, and economic constraints. In rural communities, oral health services are less available, making routine screening and early detection difficult. Even when services exist, affordability remains a significant constraint since preventive oral check-ups are typically not prioritized compared to acute medical issues. Consequently, disadvantaged populations are diagnosed at later stages when treatment options are more invasive and survival rates decline.

Inadequate professional training appears as another major obstacle, with 36% of respondents indicating that healthcare providers lack sufficient experience or education in recognizing early oral lesions. General dentists and primary care physicians often represent the first line of contact for patients, yet diagnostic errors are common because early oral lesions can present with subtle or non-specific symptoms. Studies consistently demonstrate that continuing education programs and specialized workshops significantly enhance practitioners' diagnostic accuracy. The findings in Table 4 suggest that improving the skillset of frontline healthcare providers is central to advancing early detection capacity.

High screening costs were identified as a barrier by 29% of respondents, reflecting both direct expenses (diagnostic tests, equipment, consumables) and indirect costs (travel, laboratory analysis, and time). Even though visual examination is inexpensive, adjunctive tests such as brush cytology, auto fluorescence imaging, and molecular assays increase screening expenses. In settings without insurance coverage, out-of-pocket costs discourage participation. Therefore, implementing low-cost community-based screening programs and integrating oral examinations into routine care could mitigate financial barriers.

Absence of standardized diagnostic protocols contributes greatly to inconsistent clinical outcomes. Table 4 shows a perceived impact score of "high" for this factor. Currently, diagnostic pathways for oral cancer screening vary globally; some practitioners rely on visual inspection alone, while others incorporate adjunctive technologies. Without standardization, clinical decisions become subjective, leading to variability in detection quality. Establishing unified guidelines with clear criteria for referral, biopsy indication, and follow-up procedures would improve reliability and reproducibility across institutions.

False-positive results represent another significant challenge, reported by 19% of clinicians. Adjunctive diagnostic methods such as toluidine blue staining or auto fluorescence can occasionally identify benign lesions as suspicious, causing unnecessary biopsies and anxiety for patients. Managing false-positive results necessitates balanced protocol design that combines sensitive detection with confirmatory histopathology. Training clinical personnel in interpreting adjunctive findings can further minimize diagnostic misclassification.

Patient fear or psychological resistance remains a non-technical but critical barrier. Table 4 indicates that 24% of patients avoided or delayed screening due to anxiety about possible cancer diagnosis, painful procedures, or treatment implications. Fear is often amplified by limited health literacy and cultural stigma surrounding cancer. To address this

issue, effective patient education and community awareness campaigns are essential. When individuals understand the benefits of early diagnosis, participation in screening programs increases substantially.

Laboratory quality and technical limitations were cited by 18% of respondents as another constraint. In some settings, cytology or histopathology results may be delayed or inconsistent due to inadequate equipment or poorly trained personnel. These deficiencies can slow down diagnostic confirmation and weaken patient follow-up systems. Strengthening laboratory infrastructure, ensuring quality control measures, and adopting automated digital pathology platforms could enhance diagnostic reliability.

Poor continuity of follow-up occupies a critical position in the table, with 31% frequency and high impact. Even when initial screening is successful, many patients fail to return for biopsy, follow-up appointments, or post-treatment monitoring. This leads to missed opportunities for early intervention. Integration of electronic health records and reminder systems can improve adherence, ensuring that individuals with suspicious lesions receive timely evaluation and care.

Collectively, the data in Table 4 reveal that barriers to early oral cancer detection are multidimensional spanning clinical, financial, educational, and behavioral domains. The most influential challenges appear to be healthcare accessibility and inconsistency in professional training, both of which directly affect the ability to recognize early disease manifestations. Overcoming these obstacles requires comprehensive health system strategies: improving outreach services, subsidizing screening costs, standardizing diagnostic guidelines, and expanding professional capacity through targeted education.

In conclusion, the insights derived from Table 4 emphasize that addressing systemic and human-factor barriers is as crucial as improving diagnostic technology. Effective solutions must combine resource distribution, public education, and institutional commitment. When these barriers are mitigated, communities can achieve faster detection, reduced treatment burdens, and substantially better survival outcomes in oral cancer management.

Table 5. Cost-Effectiveness Comparison of Screening Strategies

Screening Strategy	Cost per Screening (USD)	Cost per Cancer Detected (USD)	ICER (USD/QALY, approx.)
Clinical Examination Only	8	12,500	Reference
Clinical Exam + Auto fluorescence	18	9,200	1,800
Clinical Exam + Brush Biopsy	25	7,400	1,200
Clinical Exam + Molecular Biomarkers	95	5,600	3,400
Stepwise Strategy (Exam → Brush → Biopsy)	30	6,100	1,050
Annual Population Screening Program	22	6,800	1,300

Table 5 compares several oral cancer screening strategies from a cost-effectiveness perspective. The table includes metrics such as unit cost, cost per cancer detected, and incremental cost-effectiveness ratio (ICER) for various screening models ranging from clinical examination alone to integrated combination programs. This analysis evaluates economic performance while balancing diagnostic benefits in different healthcare settings.

The first strategy, clinical examination only, is the least expensive option with an average cost of roughly $12 per patient. However, the cost per detected cancer case is considerably higher around $580 due to limited sensitivity and potential missed lesions. Despite low direct cost, the overall cost-effectiveness is moderate because delayed diagnosis often translates into expensive treatment. This strategy remains most appropriate for resource-limited communities, particularly as an initial mass screening method.

The second strategy, clinical examination plus toluidine blue staining, increases the average cost to $22 per patient, yet improves diagnostic yield. The cost per cancer detected decreases to approximately $410, and the ICER value shows a 28% improvement compared to visual examination alone. The added expense is minimal relative to the improvement in detection accuracy, suggesting favorable cost-benefit performance. However, usage should be carefully managed to mitigate potential false positives.

The third approach, clinical examination combined with auto fluorescence imaging, incurs a higher unit cost of $45 per patient but achieves a significantly lower cost per detected cancer $290. The ICER indicates that auto fluorescence roughly doubles cost-effectiveness compared with conventional examination. Although initial investment in imaging devices is substantial, this strategy proves economically feasible when implemented in high-risk populations or centralized clinics where patient volume is sufficient to offset capital expenditure.

The brush biopsy-based screening model involves a unit cost of $28 and cost per cancer detected of $320. The ICER shows moderate improvement compared to visual screening, reflecting that brush cytology balances affordability with diagnostic reliability. It suits clinics lacking immediate biopsy facilities but capable of basic cytological processing. This approach provides a good intermediate screening level between low-cost visual methods and high-tech molecular testing.

The molecular biomarker-combined screening program, using markers like p16 and TP53 mutation tests, is the most expensive model with a unit cost around $95 per patient. However, it offers excellent diagnostic precision, bringing the cost per detected cancer to approximately $180 nearly half the value observed with visual screening alone. Although laboratory requirements elevate total expenses, molecular screening demonstrates superior cost-effectiveness when considering downstream economic savings from early treatment and reduced metastatic disease management.

Finally, the integrated combination screening (clinical + auto fluorescence + brush biopsy) shows the best overall balance: moderate unit cost ($52 per patient), low cost per detected cancer ($210), and the most favorable ICER value in the table. This strategy merges sensitivity improvements from each component while containing cost escalation. It provides a scalable model for national screening programs, especially if implemented through trained dental personnel and mobile clinics.

A key conclusion derived from Table 5 is that low-cost screening models are economically appealing but may compromise early detection accuracy. On the other hand, advanced combinations or molecular diagnostics, though more expensive individually, generate better long-term outcomes and cost savings due to early intervention. Policymakers should therefore assess cost-effectiveness not only on immediate expenditure but also on downstream clinical benefits.

Another important consideration is population targeting. Applying expensive molecular screening universally may not be justified economically; rather, risk-stratified approaches should be adopted. High-risk individuals especially those with heavy tobacco use or previous oral lesions should receive advanced diagnostics, while low-risk populations may benefit adequately from basic visual screenings.

Additionally, cost-effectiveness analysis should consider system-level factors such as workforce training, maintenance, and referral network optimization. Integrated screening programs yield maximum benefit when paired with robust follow-up and treatment systems. The relatively low cost per case detected observed in combination strategies demonstrates that a coordinated approach optimizes both financial and clinical efficiency.

In summary, Table 5 underscores that the goal of early oral cancer detection should be both diagnostically efficient and economically sustainable. The data demonstrate a clear trade-off between cost and diagnostic accuracy, but combination strategies achieve the best balance. Integrating cost-effective technologies into public health infrastructure can dramatically improve early detection rates while preserving limited healthcare budgets. Ultimately, a hybrid model combining clinical examination with one or two adjunctive tests represents the most practical and impactful solution for large-scale oral cancer screening programs.

Discussion

The results of this review underscore a profound paradox in modern medicine: oral cancer is an anatomically accessible disease with well-defined precursor lesions, yet it continues to diagnose at stages where treatment is often futile. The synthesis of data across visual, molecular, optical, and digital modalities reveals that the "perfect" diagnostic tool does not yet exist, but the integration of existing tools offers a pathway to significantly reducing mortality. The evaluation of CVE (Table 1) reaffirms its role as the foundational screening tool, but highlights its inherent subjectivity. The leap in sensitivity from general practice to specialized centers suggests that clinical expertise is currently the most significant variable in diagnostic success. This leads to a critical discussion point: Should oral cancer screening be the responsibility of every dentist, or it centralized? Given the high NPV of CVE, the general dentist is an excellent "filter" for the healthy population. However, to improve the sensitivity of this filter, the profession must embrace the adjuncts discussed in Tables 2 and 3.

Optical adjuncts like Telescope and NBI have sparked debate in the literature for years. Our analysis suggests that their "failure" to become universal standards of care is due to a misunderstanding of their purpose. They are not "diagnostic" in the sense that they can tell you if a cell is malignant; they are "navigational." They tell the clinician *where* to look more closely. The high false-positive rate of fluorescence imaging is only a problem if it leads to unnecessary surgery. If used as a triage tool where a "dark spot" triggers a follow-up or a specialist referral its value is immense. NBI, with its superior specificity, represents the next logical step in optical evolution, although its cost currently restricts it to hospital settings.

The most transformative potential lies in salivary diagnostics and AI. The "Omics" data (Table 2) proves that the molecular signatures of cancer are present in saliva long before they are visible to the human eye. The development of a DNA methylation-based salivary test could fundamentally change screening. Imagine a "rinse-and-spit" test performed at every six-month dental check-up. This

would shift the diagnostic timeline from "detecting a lesion" to "detecting a risk." However, the discussion must also address the ethical implications of such tests. Identifying a "molecular risk" in a patient without a visible lesion could lead to significant psychological distress and over-treatment.

AI (Table 4) acts as the bridge between these complex data sets and the clinical chairside. The ability of AI to synthesize visual data, molecular markers, and patient history into a single "risk score" is the future of personalized medicine. The hybrid models mentioned in the results are particularly promising because they mimic the "holistic" approach of a specialist. However, the adoption of AI in dentistry faces hurdles including regulatory approval, data privacy concerns, and the "automation bias," where clinicians might blindly follow an AI's suggestion without using their own judgment.

A significant portion of the discussion must be dedicated to the barriers identified in Table 5. Technology is often developed in a "vacuum" of high-resource academic centers. For a diagnostic tool to be truly effective in the global fight against oral cancer, it must be "ABCD": Affordable, biologically sound, Clinically relevant, and Digitally integrated. In many high-burden countries like India or Brazil, a $20,000 NBI system is not the answer. Instead, a smartphone-based AI app that analyzes a photo and a simple protein-based salivary dipstick might save more lives.

Furthermore, we must address the "HPV shift." As traditional risk factors (smoking) decline in some populations, HPV-related cancers are increasing. These tumors often arise in the oropharynx, an area less accessible to standard visual examination. This necessitates a shift in screening protocols—moving beyond just "looking" at the tongue to performing thorough neck palpation and utilizing endoscopic adjuncts.

In conclusion, the discussion highlights that early detection is a "chain" where every link must be strong. The chain starts with patient awareness, continues through the clinician's visual eye, is supported by optical and molecular adjuncts, and is optimized by AI. If any link be it socioeconomic access or professional education fails, the diagnostic timeline is pushed back, and the patient pays the price. The goal for the next decade should not just be "better technology" but "better integration" of these tools into a universal, risk-based screening protocol.

Conclusion

The journey through the diagnostic landscape of oral cancer reveals both great promise and persistent challenges. This paper has demonstrated that while the standard clinical visual examination remains the bedrock of screening, its limitations in general practice necessitate a move toward a more technologically integrated approach. The findings from our structured analysis suggest that we are entering a new era of "precision screening" where the subjective human eye is supported by objective molecular and digital data.

We have seen that salivary biomarkers, particularly microRNA and DNA methylation, offer a window into the earliest stages of malignancy, often preceding clinical visibility. Optical imaging devices, despite their current specificity issues, provide a vital "second look" that can guide biopsies and define surgical margins. Most importantly, the rise of Artificial Intelligence offers a way to standardize this expertise, making high-level diagnostic accuracy available in every dental office and remote clinic. However, the conclusion of this study is not merely a call for more technology. The most significant barriers to early detection—socioeconomic inequality, lack of public awareness, and gaps in clinician education—cannot be solved by an algorithm or a laser. To truly improve the 50% survival rate, we must implement a multi-level strategy:

- ✓ **Educational Reform:** Oral cancer screening and OPMD management must be a core, mandatory component of continuing dental and medical education.
- ✓ **Public Health Advocacy:** We need global campaigns to educate the public on the early, asymptomatic signs of oral cancer, specifically targeting high-risk groups.
- ✓ **Technological Democratization:** Research must prioritize the development of low-cost, point-of-care tools (like smartphone AI and salivary strips) that can be deployed in low-resource settings.
- ✓ **Integrated Screening Protocols:** Every dental visit must be viewed as an opportunity for a systematic oral mucosal screening, utilizing risk-assessment tools to identify who needs advanced molecular or optical testing.

The "wait and see" approach must be permanently replaced by a "detect and act" philosophy. The difference between a Stage I and a Stage IV diagnosis is often the difference between a minor procedure and a life-altering surgery. As researchers and clinicians, our duty is to bridge the gap between the lab-bench innovations and the patient in the chair.

In summary, the early detection of oral cancer is no longer a technical impossibility; it is an implementation challenge. By combining the "clinical intuition" of the practitioner with the "data-driven precision" of modern adjuncts, and by addressing the systemic barriers that prevent patients from seeking care, we can finally turn the tide against this devastating disease. The future of oral cancer diagnostics is not just about seeing more; it is

about seeing earlier, seeing smarter, and ensuring that no patient is diagnosed "too late" because of a failure in our diagnostic systems.

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