

Beyond the Visible: Early Detection of Oral Cancer from the Dental Chair to the Algorithm: *A Narrative Review*

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Abstract: ***Background:** The mouth is one of the most obvious cancer sites to check and the clinician can see directly the cancer, but oral cancer is still too often found late, when treatment is more complex and survival poorer. The delay in recognition and referral, poor access to trained examiners and the silent early behaviour of precursor lesions all contribute. **Objective:** To assess current and emerging strategies for the early detection of oral cancer from oral examination to artificial intelligence and to be clear about what the evidence does and does not support. **Approach:** Narrative synthesis of recent guidelines, systematic and scoping reviews, a landmark randomised screening trial, and selected primary studies. **Findings:** Systematic visual examination is still the only approach with randomised evidence of a mortality benefit, and it was found to be greater in tobacco or alcohol smokers. Adjunctive devices, such as vital staining, light-based aids and cytology can help to prioritize lesions, but can't replace biopsy and there's not been any evidence that they have been recommended or applied in a routine way for screening. Salivary biomarkers, liquid biopsy, biosensors and image-based artificial intelligence are all scientifically fascinating and sometimes very accurate, but most evidence comes from small, single-centre studies that don't have external validation. **Conclusions:** Early detection will be based less on any one gadget than on a risk-aware approach: a thorough assessment for every adult, targeted screening of high-risk groups, structured surveillance of potentially malignant disorders, timely biopsy of suspicious lesions and well-validated decision-support tools that will be used to enable wider access rather than to replace clinical judgement.*

Keywords: oral cancer; oral squamous cell carcinoma; early detection; oral potentially malignant disorders; screening; saliva biomarkers; artificial intelligence

1. Introduction

Few cancers offer clinicians such a generous head start. The oral cavity is visible, felt and photographed without a single incision and far too many patients arrive with disease that has already reached the neck. Part of the reason is human: a painless white patch is easy to ignore, and a non-healing ulcer is easily pinned on a sharp tooth. Part of it is structural: long journeys to reach a trained examiner and further delays between a first visit and a specialist appointment [4,5]. The scale of the problem is considerable. GLOBOCAN 2022 estimated there were roughly 390,000 new cases of lip and oral cavity cancer and about 188,000 deaths worldwide in 2022. Over the wider group of lip, oral cavity and pharyngeal cancers, there were about 758,000 people diagnosed in 2022, and cancer of the oral cavity accounted for roughly 42% of them [2]. The burden is not evenly spread around the world. South and South-East Asia had 177,258 incident cases and 98,735 deaths from oral cancer in 2022, 52% of all oral cancer deaths globally, with the highest age-standardised rates in men in India, Sri Lanka, Bangladesh and Pakistan [3]. With new information, we expect the annual number of cases to increase from around 390,000 in 2022 to about 600,000 by 2045 [4]. In such circumstances, early detection is not an academic nicety; it is one of the few levers that can still change outcomes. In this review, we walk through the detection toolkit in the order a patient might meet it: who is at risk, what a careful examination can achieve, what adjunctive devices add, what molecular and digital technologies promise, and how these pieces might fit together in practice.

2. Scope and Approach

This is a narrative review. We focused on recent clinical guidelines, systematic and scoping reviews, randomised evidence, and primary studies that illustrate emerging technologies, and we particularly focused on oral cavity-specific evidence. When we discuss the findings from head and neck settings, we say so.

3. Knowing the runway: potentially malignant disorders and risk

Oral squamous cell carcinoma is not always detectable, but it often has a start. Oral potentially malignant disorders (OPMDs) are the most important precursors to oral cancer [6], and the way they act is not uniform in character. The most common OPMD which has been found in the literature is oral leukoplakia with a pooled malignant transformation rate of 6.64% (95% CI 5.21 to 8.21) in a meta-analysis of 55 studies and 41,231 patients, although heterogeneity was very high ($I^2 = 96.7\%$) [6]. The rates of transformation were higher in smokers, in lesions on the lateral side of the tongue, and in epithelial dysplasia [6]. Other disorders are at very different risk levels. An earlier meta-analysis of 92 studies reported an overall OPMD transformation rate of 7.9%, with lichen planus at the low end, and erythroplakia and proliferative verrucous leukoplakia at the high end [7]. An umbrella review also found around half of cases to transform in proliferative verrucous leukoplakia versus about 6% for conventional leukoplakia [8]. The point is that one quoted "rate" can be misleading. A small homogeneous leukoplakia in a non-smoker and an erythroplakic patch on

the floor of the mouth in a heavy tobacco user are not the same clinical problem, and surveillance intensity should reflect that.

4. The oldest tool still earns its keep: examination and visual screening

4.1 What the Kerala trial taught us

The strongest evidence for screening comes from the Kerala cluster-randomised trial, in which trained health workers examined the mouth over repeated rounds and referred people with suspicious findings [9]. In the original analysis, oral cancer mortality was 34% lower among ever-users of tobacco or alcohol, with no apparent benefit in never-users [9,11]. Follow-up extended to 15 years, and the reduction in the high-risk group remained statistically significant, at about 24% in the Cochrane synthesis of the trial [10,25]. A later risk-based reanalysis found that the gain from screening rose with predicted baseline risk, so the people at highest risk benefited most [11].

Two lessons follow. First, visual screening can work when it is organised, repeated and targeted. Second, it works best where the disease is concentrated. Economic modelling from India points the same way, suggesting that screening high-risk individuals is an attractive strategy for resource-constrained health systems [12]. It is worth remembering that this single trial remains the only randomised study of oral cancer screening with a mortality endpoint [11].

4.2 The clinical oral examination in everyday practice

The American Dental Association's living guideline series reflects a pragmatic position. Its good practice statements urge clinicians to perform a clinical oral examination in all adult patients and to explain to patients why the examination matters, including the early detection of mucosal abnormalities such as OPMDs and oral cavity cancer [13]. In other words, before any device is considered, the examination itself is the intervention. Training, calibration and a habit of looking at the tongue borders, floor of mouth and soft palate matter more than any gadget on the tray.

5. Adjuncts: a helpful torch or false comfort?

Chair-side adjuncts have long been marketed as ways to sharpen the clinician's eye. They include vital staining with toluidine blue, brush cytology, chemiluminescence, tissue autofluorescence and narrow-band imaging. The honest summary is that enthusiasm has outrun evidence.

The research on these aids is patchy and inconsistent, which makes firm conclusions hard, and guidelines have grown correspondingly cautious. A recent living guideline suggests against using cytology as a screening adjunct in asymptomatic adults whose mouths look normal [13], and the American Dental Association advises against using certain saliva- or light-based tools to judge whether a lesion is malignant [14]. A systematic review found high heterogeneity and no randomised trials of adjunctive aids [15], and the Cochrane review of screening found no evidence to support toluidine blue, brush biopsy or

fluorescence imaging for reducing oral cancer mortality [25]. Put plainly, they are not yet reliable enough to carry the weight clinicians sometimes ask of them.

What is missing is evidence from the settings where these devices are actually used. A prospective study has been planned to compare autofluorescence and toluidine blue against biopsy in people with oral potentially malignant disorders in routine primary care, precisely because that evaluation has not been done before [16]. A recent review of diagnosis and monitoring reaches a similar view: adjuncts can be useful, but they cannot replace a proper tissue diagnosis [17]. In practice, these tools can point us in the right direction, but they should never become a reason to delay a biopsy when a lesion looks or behaves suspiciously.

6. Beyond the surface: saliva, liquid biopsy and biosensors

Saliva is an attractive diagnostic fluid. It can be collected without a needle, as often as needed and at low cost, and interest in salivary tests for early oral cancer has grown quickly. Some groups are building point-of-care devices that would analyse samples at the chair side instead of in a distant laboratory, while others are pairing genomic analysis with machine learning to make sense of the large datasets these samples generate, including fragments of circulating tumour DNA in liquid-biopsy approaches [17,19]. The hope is to catch disease when it is easier to treat. For now, the evidence is still developing.

Volatile organic compounds have drawn particular attention. One study applied machine learning to breath samples to predict oral squamous cell carcinoma [20], and another used artificial neural networks on salivary volatile profiles and reported perfect sensitivity and specificity [21]. Numbers like these deserve a closer look rather than immediate celebration. The studies were small: the saliva work analysed only 30 to 50 samples and the breath study 105 [20,21]. More broadly, methods differ between laboratories, pre-analytical handling varies, and thresholds and validation are not standardised [17]. Biosensors and AI-powered platforms are promising, but they remain at an early stage of development and need much more work before routine use.

7. Teaching Machines to Look: Artificial Intelligence

The central problem is that too few people are examined by a trained expert. Could a smartphone and a dependable algorithm help close that gap? A recent scoping review screened 88 studies of artificial intelligence for early oral cancer diagnosis and included 28, most of them from South and South-East Asia, where the need is greatest [4]. The inputs ranged from smartphone photographs and clinical images to saliva and breath samples, and deep convolutional neural networks gave the strongest sensitivity, specificity and accuracy [4].

Some results are encouraging. A deep learning model assessing clinical images for oral premalignant disorders and oral cancer reached an accuracy of 88.6%, with a sensitivity

of 91.3% and a specificity of 86.4%, as summarised in the scoping review [4]. Mobile-based tools also allow screening in community settings, which matters most for high-risk groups [23]. Not every approach performs as well. An artificial neural network that predicted oral cancer from clinical and epidemiological data found most cases (sensitivity 85.71%) but struggled to exclude non-cases (specificity 60%), and its confidence intervals were wide because the dataset was small [24]. It is a useful reminder that the data fed into a model matter as much as the model itself.

There are real caveats. Many studies relied on small samples or data from a single site, and few tested whether their results hold in other populations or with different image

types. Algorithmic bias and the opacity of “black box” systems are further concerns, along with standardised image capture, data privacy and training for the clinicians who would use these tools [4,5]. The authors of the scoping review call for larger studies and clear rules before AI is used routinely in clinics [4]. We agree: AI should support decisions and widen access to care, not replace the clinician who examines the patient.

8. Comparing the options

Table 1 condenses the evidence for each approach and an overall judgement of maturity.

Table 1: Early detection approaches for oral cancer: contribution, evidence and maturity

Approach	What it offers	Evidence and main limitations	Maturity
Conventional oral examination (COE) / visual screening	Low cost; feasible for trained community health workers; directly inspects the mucosa	Only randomised mortality evidence in oral cancer (Kerala); benefit concentrated in tobacco/alcohol users [9-11]. Examiner-dependent.	Established
Vital staining (toluidine blue)	Chair-side aid to highlight suspicious areas	Being tested against biopsy in primary care [16]; evidence base limited by heterogeneity [15]	Adjunct
Light-based aids (autofluorescence, chemiluminescence, narrow-band imaging)	Visual contrast to guide lesion assessment and biopsy-site choice	Systematic review: high heterogeneity, no randomised trials [15]; ADA summary advises against use to evaluate lesions for malignancy [14]	Adjunct, contested
Brush cytology	Minimally invasive sampling of a visible lesion	Guideline panel suggests against use as a screening adjunct in asymptomatic adults with no visible abnormality [13]	Adjunct, restricted
Saliva and breath biomarkers, liquid biopsy	Non-invasive; repeatable; suited to monitoring	Small samples, pre-analytical variability, inconsistent thresholds, little external validation [4,17,20,21]	Developmental
Biosensors and point-of-care platforms	Rapid, low-cost measurement of salivary markers	Promising scoping-level evidence [19]; largely developmental [17]	Developmental
Artificial intelligence (image, cytology, spectral analysis)	Scalable triage; smartphone-based screening; reduces reliance on specialist availability	Deep CNNs perform best; small, single-site datasets and scarce external validation [4,22-24]	Emerging

Numbers in brackets refer to the reference list. CNN, convolutional neural network.

9. Bringing it together: a risk-aware pathway

Drawing on the evidence above, we propose a stepwise approach that is consistent with existing guidelines. It is our own interpretation rather than a formally validated pathway.

- 1) **Examine every adult.** A careful oral examination should be a routine part of care for every adult, and patients should understand why it matters [13].
- 2) **Target the high-risk.** Organised, repeated visual screening by trained health workers is most worthwhile for tobacco and alcohol users and other high-risk groups [9-12].
- 3) **Watch precursor lesions closely.** When monitoring potentially malignant disorders, weigh the type, size and site of the lesion, the presence of dysplasia and the patient's risk behaviours, rather than applying one-size-fits-all surveillance [6-8].
- 4) **Biopsy what looks suspicious.** Adjuncts may help decide priorities or where to sample, but examining the tissue remains the most reliable route to a diagnosis [14,17].
- 5) **Use technology to widen access.** AI and point-of-care tools can support decisions where specialists are scarce, provided they have first been independently validated [4,19].

10. Challenges and future directions

Several hurdles stand between new technology and better outcomes. The first is the quality of the evidence: there are no randomised trials of adjuncts, and the studies that exist vary widely in design [15], while molecular and digital tools lack external validation [4,17]. The second is context. A device that performs well in a specialist clinic may not do so in primary care, which is where it is most needed [16]. The third is equity. Because most of the burden falls in South and South-East Asia [3], tools must be affordable, robust and culturally acceptable there, not merely accurate in a well-funded research centre.

Looking ahead, the most credible path is integration. Progress in early diagnosis and monitoring will most likely depend on models that combine clinical examination, adjunctive imaging, minimally invasive sampling, molecular biomarkers and computational decision support, validated in prospective multicentre studies [17]. Risk models that identify who benefits most from screening [11], primary care trials of adjuncts [16], explainable and bias-aware AI [4], and point-of-care biosensors [19] are the areas where the next decade of useful research is likely to lie.

11. From evidence to practice: training, referral and awareness

11.1 Making the pathway work

A pathway on paper is only as good as the people and systems that carry it out. The Kerala trial worked because trained health workers examined people in their own communities, in repeated rounds, and had a clear route for referring anyone with a suspicious finding [9]. The Cochrane review of screening reached a practical conclusion of its own: until more trials exist, opportunistic visual screening by appropriately trained dentists and oral health practitioners is recommended for all patients, particularly those who use tobacco, alcohol or both [25]. Both lessons point to the same priorities: training, calibration of examiners, and a dependable referral route.

Delay can arise at several points: the patient who ignores a painless patch, the clinician who treats a persistent ulcer as trauma, and the weeks that pass between a first visit and a specialist appointment [4,5]. Each step is a chance to lose a patient. Simple measures help: a shared definition of what counts as a lesion needing referral, a clear time frame for review of any ulcer that has not healed, and feedback to the referring clinician once a biopsy result is available. Pairing a trained examiner with a smartphone image that a specialist can review remotely is one way digital tools could shorten the path without replacing the examination itself [5,23].

Patients are part of the pathway too. Tobacco and alcohol users are the people who gain most from screening [9,11], yet they may be the least likely to attend a routine dental visit. Explaining why the examination matters, as the ADA good practice statements urge [13], and taking it to where high-risk groups already are, such as community camps and primary care clinics, deserves as much attention as any new device.

11.2 Limitations of this review

This was a narrative review rather than a systematic one. We did not run a registered protocol or a formal risk-of-bias assessment, and we gave priority to recent guidelines, systematic reviews and illustrative primary studies, so relevant work may have been missed. Several of the technologies discussed are changing quickly, and some of the accuracy figures quoted come from small, single-centre studies, as noted above. The proposed pathway in Section 9 is our interpretation of the evidence and has not been validated in a prospective study. These limits do not alter the central message, but they do argue for reading the numbers with care.

12. Conclusion

Oral cancer is one of the few cancers we can look for with our own eyes, and finding it early saves lives. The approach with the strongest evidence is also the simplest: a careful examination for every adult, repeated screening of high-risk groups, and structured follow-up of suspicious lesions. Stains, light-based aids, saliva tests and AI may yet earn a place in routine care, but they need rigorous testing in real-

world settings before we lean on them. Until then the goal is plain: find the disease early, biopsy promptly, and make sure no patient slips through the cracks because of a delayed diagnosis.

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