# Miscellaneous Diagnostic Procedures

**Policy Number**: DCP040.10
**Effective Date**: January 1, 2025

Instructions for Use

**Table of Contents** **Page**



**Related Dental Policy**

- Salivary Testing

## Coverage Rationale

### In-Office HbA1c and Blood Glucose Level Tests

**For the purposes of diagnosing pre-diabetes and diabetes, using HbA1c and blood glucose level tests in the dental office setting are not indicated due to insufficient evidence of efficacy or improved health outcomes.**

### Caries Susceptibility Tests

**Caries susceptibility tests are not indicated due to insufficient evidence of efficacy.**

### Adjunctive Pre-Diagnostic Tests That Aid in the Detection of Mucosal Abnormalities Including Premalignant and Malignant Lesions

**These procedures are not indicated due to insufficient evidence of efficacy.**

### Brush Biopsy

**Brush biopsies are not indicated due to insufficient evidence of efficacy.**

### Pulp Vitality Tests

**Pulp vitality tests are indicated for the following:**

- For traumatic injuries to teeth
- Teeth with deep Caries or defective restorations

**Pulp vitality tests are not indicated for the following:**

- Sensitivity of exposed dentin without evidence of Pulp pathosis
- As part of routine dental examinations

### Diagnostic Casts

**Diagnostic Casts may be indicated for a more thorough evaluation of the following:**

- Tooth interdigitation
- Functional occlusion, and any occlusal abnormalities
- Wear facets and defective restorations, coronal contours, proximal contacts, and embrasure spaces between teeth

## Antigen and Antibody, and Molecular Testing

**Antigen and Antibody testing for public health related pathogens is out of scope for dental providers within the dental office.** Refer to the Description of Services section.

# Definitions

**Antibody**: A substance produced by B lymphocytes in response to a unique Antigen.

**Antigen**: Any substance capable of eliciting an immune response or of binding with an Antibody.

**Caries**: Commonly used term for tooth decay.

**Diagnostic Cast**: A replica of teeth and adjoining tissues created digitally or by a casting process (e.g., plaster into an impression). "Study model" is another term used for such a replica.

**HbA1c/A1C**: A blood test measures average blood glucose (blood sugar) control for the past 2 to 3 months.

**Pulp**: Connective tissue that contains blood vessels and nerve tissue which occupies the Pulp cavity of a tooth.

# Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

| CDT Code | Description |
|---|---|
| D0411 | HbA1c in-office point of service testing |
| D0412 | Blood glucose level test – in-office using a glucose meter |
| D0425 | Caries susceptibility tests |
| D0431 | Adjunctive pre-diagnostic test that aids in detection of mucosal abnormalities including premalignant and malignant lesions, not to include cytology or biopsy procedures |
| D0460 | Pulp vitality tests |
| D0470 | Diagnostic casts |
| D0604 | Antigen testing for a public health related pathogen, including coronavirus |
| D0605 | Antibody testing for a public health related pathogen, including coronavirus |
| D0606 | Molecular testing for a public health related pathogen, including coronavirus |
| D7288 | Brush biopsy - transepithelial sample collection |



# Description of Services

Pulp vitality testing involves thermal or electrical stimulation of a tooth to aid in the diagnosis of pulpal pathology, indicating the need for endodontic therapy.

Diagnostic Casts or study models are stone models made from impressions of the dentition. They are inclusive in most restorative, prosthodontic and orthodontic treatment planning, however they can have use in select cases for complex treatment planning.

Caries susceptibility testing can be done with a variety of diagnostic tools. Products include testing for bacteria levels, buffering capacity of saliva, and a device called CariScreen (Oral Biotech) that screens plaque samples for bacteriologic activity using adenosine triphosphate (ATP) driven bioluminescence.

There are several adjunctive tests to aid in the detection of mucosal abnormalities using lights, dye, and brush biopsy devices. There is a lack of evidence to support or refute the efficacy of these devices and a traditional physical and tactile

examination, with histopathological examination of suspicious lesions via surgical biopsy remains the “gold standard” for detecting oral cancer (Rethman et al. 2010). Additionally, concern has been raised about the delay of a cancer diagnosis for positive and negative results, as all lesions require a scalpel biopsy for a definitive diagnosis.

Many patients visit their dentist more often than their primary care providers, and as periodontal disease is associated with diabetes, the clinical utility of chairside dental office screening with subsequent referral to primary care has been explored as a means to improve the diagnosis of prediabetes and diabetes and reducing associated comorbidities. Blood glucose level testing may be indicated as a presurgical screening procedure in certain surgical situations, or when patients exhibit symptoms of hyperglycemia, and all dental offices should have a protocol for managing hypoglycemic episodes in conscious and unconscious patents.

Coronaviruses are a group of viruses that are known to cause respiratory illnesses ranging from the common cold to more severe disease. In late 2019, the World Health Organization was notified of a rapidly growing outbreak of a severe lower respiratory tract disease. In February 2020, the International Committee on Taxonomy of Viruses named this new virus Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). On March 11, 2020 it was declared a pandemic by the World Health Organization. In 2020, the American Dental Association (ADA) supported the use dentists who chose to participate in diagnostic testing, vaccine administration and other ancillary procedures to expand national efforts during declared local, state, or federal public health emergencies. On May 11, 2023, the federal Public Health Emergency (PHE) for COVID-19, declared under Section 319 of the Public Health Service (PHS) Act expired.

# Clinical Evidence

## HbA1c Testing and Blood Glucose Level Testing

In a 2020 systematic review and meta-analysis, Chinnasamy et al. summarized the data on the prevalence of undiagnosed type 2 diabetes mellitus (T2DM) and prediabetes amongst dental patients and further explore the effectiveness of the point of care (PoC) screening and its implication for use in the dental setting. Studies were eligible for inclusion if they were cross-sectional in design and used PoC screening for undiagnosed DM or hyperglycemia in the dental setting via (HbA1c), and the results of the PoC screening test were confirmed with official testing not in the dental setting. Nine studies met the authors inclusion criteria. The results showed the prevalence of T2DM and prediabetes in the dental setting to be 11.23% and 47.38% respectively, and the authors concluded that targeted PoC screening in the dental setting is a novel approach that could potentially help reduce undiagnosed disease, however more research is needed before the utility can be demonstrated.

Mataftsi et al (2019) conducted a study to implement a chairside diabetes screening strategy for the identification of undiagnosed hyperglycaemia in periodontal patients. Measurement of HbA1c was performed in 139 patients diagnosed with periodontal disease to determine possible unknown hyperglycaemia. Patients fulfilled the criteria for screening according to the questionnaire by the Centers for Disease Control and Prevention (CDC). The Cobas® b101 in vitro diagnostic system was used for the measurement of glycosylated haemoglobin (HbA1c) in capillary blood. Body mass index (BMI) and waist circumference were also measured to determine splanchnic obesity. Periodontal parameters were assessed with an automated probe and included probing depth, clinical attachment loss, bleeding on probing and presence/absence of plaque. Most patients had moderate periodontitis, and the results showed that almost 25% of the subjects tested were found to have unknown hyperglycaemia while 80.5% of them had splanchnic (abdominal) obesity. A significant association was found between HbA1c and BMI (Mann-Whitney test; $p = 0.0021$) as well as between HbA1c and waist circumference (Spearman rho test; $p = 0.0007$). No differences were observed regarding periodontal parameters between subjects exhibiting HbA1c ≥ 5.7% and those with HbA1c < 5.7% (Mann-Whitney test; $p > 0.05$) although those with HbA1c ≥ 5.7% displayed higher proportions of sites with clinical attachment loss > 5 mm (z test with Bonferroni corrections; $p < 0.05$). The authors concluded that periodontal patients, especially those with a bigger than normal BMI and waist circumference, may be target group worth screening for diabetes.

Teeuw et al. (2017) conducted a study on the use of diabetic screening on patients with diagnosed periodontal disease. A total of 313 individuals from a university dental clinic participated. From 126 patients with mild/moderate periodontitis, 78 patients with severe periodontitis and 109 subjects without periodontitis, HbA1c values were obtained by the analysis of dry blood spots. Differences in mean HbA1c values and the prevalence of (pre)diabetes between the groups were analyzed. The mild/moderate and severe periodontitis groups showed significantly higher HbA1c values (6.1% ±1.4% (43 mmol/mol ±15 mmol/mol) and 6.3% ±1.3% (45 mmol/mol ±15 mmol/mol), respectively) compared with the control group (5.7% ±0.7% (39 mmol/mol ±8 mmol/mol), $p = 0.003$). In addition, according to the American Diabetes Association (ADA) guidelines for diagnosis, there was a significant overrepresentation of subjects with suspected diabetes (23% and 14%) and pre-diabetes (47% and 46%) in the severe periodontitis group and mild/moderate periodontitis groups, respectively, compared with the control group (10% and 37%, $p = 0.010$). Notably, 18.1% of patients with suspected new diabetes were

found among subjects with severe periodontitis compared with 9.9% and 8.5% among subjects with mild/moderate periodontitis and controls, respectively (p = 0.024). Conclusions: The dental office, with particular focus on patients with severe periodontitis, proved to be a suitable location for screening for (pre)diabetes; a considerable number of suspected new diabetes cases were identified. The early diagnosis and treatment of (pre)diabetes help to prevent more severe complications and benefit the treatment of periodontitis.

Lalla et al. (2015) conducted a randomized clinical trial to assess an approach to improving behavioral and glycaemic outcomes in dental patients who present with diabetes risk factors and previously unrecognized hyperglycaemia. The authors randomized 101 individuals identified with potential diabetes or pre-diabetes into two interventions. In the basic/control intervention, participants were informed about their diabetes risk factors and blood test result and advised to see a physician. In the enhanced/test intervention, patients received a detailed explanation of findings and their implications, a written report for the physician, and were contacted at 2 and 4 months to inquire whether medical follow-up had occurred. At a 6-month re-evaluation, outcome measures included visit to physician, positive lifestyle changes and reduction in HbA1c. 73 subjects returned for the 6-month reevaluation, and the results showed that the two intervention groups did not significantly differ in any of the outcome variables. Eighty-four percent of subjects reported having visited a physician post-randomization, and 49% reported at least one positive lifestyle change as a result of our intervention. In subjects identified with potential diabetes (baseline HbA1c ≥ 6.5%), HbA1c was reduced 1.46 ±0.28% compared to baseline (p < 0.01). The authors' concluded that diabetes risk assessment and education by dental professionals of affected individuals unaware of their status may contribute to improved patient outcomes. This study is limited to a small amount of participants.

In a 2014 field study, Genco et al. sought to assess the feasibility of screening for diabetes and prediabetes in dental practices, and in a community health center. Dental patients 45 years and older who were not aware of their diabetic status underwent evaluation for diabetes risk with an American Diabetes Association Diabetes Risk Test and with hemoglobin (Hb) A1C measurement. (Participants with an HbA1c level of 5.7 percent or greater were referred to their physicians for diagnosis). Of the 1,022 patients screened, 416 (40.7 percent) had an HbA1c blood level of 5.7 percent or greater and were referred for diagnosis. The HbA1c and the American Diabetes Association Diabetes Risk Test were correlated. Of the 416 participants who were referred, 35.1 percent received a diagnosis from their physicians within one year; 78.8 percent of these patients were seen in the community health center and 21.4 percent were seen in private dental offices. The diagnoses were diabetes (12.3 percent of patients), high risk of developing diabetes (that is, prediabetes) (23.3 percent) and no diabetes (64.4 percent). The study results show that screening for prediabetes and diabetes is feasible in a dental office, with acceptance by the dentist and dental office staff members, patients' physicians, and patients. Patients from the community health center demonstrated good compliance with referrals to physicians; however, compliance was poor among those in the private dental offices.

## Caries Susceptibility Tests

Rechmann et al. (2019) conducted a study to evaluate if readings using an adenosine triphosphate bioluminescence (ATP-B) meter (CariScreen Testing Meter, Oral BioTech) are significantly different for patients with low, moderate, and high caries risk assessed by the Caries Management by Risk Assessment Practice-Based Research Network study. Twenty practice-based research network dentists enrolled 460 patients; 271 returned for 2 or more semiannual follow-up visits over 2 years. Dentists were trained and calibrated to perform ATP-B testing and caries risk assessment (CRA) using established protocols. ATP-B readings were compared via CRA category (low, moderate, high). The results showed median ATP-B readings did not differ statistically significantly by clinician-assessed caries risk level. The authors concluded that ATP-B is poorly predictive of caries risk and future outcomes. CRA incorporates multiple risk factors, disease indicators and protective measures, and has superior predictive performance.

Gilbert et al (2014) Mutans streptococci (MS) are one of the major microbiological determinants of dental caries. The objectives of this study are to identify distinct MS and Non-MS Streptococci strains that are located at various sites and non-carious enamel surfaces in children with severe early childhood caries (S-ECC), and assess if cariogenic MS and non-cariogenic streptococci might independently exist as primary bacterial strains on distinct sites within the dentition of individual children. Dental plaque from 20 children aged 3-6 with S-ECC was collected from carious lesions (CLs), white spot lesions (WSLs) and non-carious enamel surfaces. Streptococcal isolates from each site were subjected to polymerase chain reaction (PCR) to identify MS, and arbitrarily primed-PCR for assignment of genetic strains. Primary strains were identified as ≥ 50% of the total isolates surveyed at any site. In several cases, strains were characterized for acidity using ATP-driven bioluminescence and subjected to PCR-determination of potential MS virulence products. Identification of non-MS was determined by 16S rRNA gene sequencing. The results showed 64 independent MS or non-MS streptococcal strains identified. All children contained 1-6 strains. In 11 patients, single primary MS strains were identified throughout the dentition. In 4 patients, primary MS strains were identified within CLs that were distinct from primary strains found on enamel. Streptococcus gordonii strains were identified as primary strains on enamel or WSLs in four children, and in general were less acidic than MS strains. The authors concluded that many children with S-ECC

contained only a single primary MS strain that was present in both carious and non-carious sites. In some cases, MS, and non-cariogenic S. gordonii strains were found to independently exist as dominant strains at different locations within the dentition of individual children, and the acidic potential (using ATP-driven bioluminescence) of these strains may influence susceptibility in the development of CLs.

Hallett et al (2013) Conducted a study to evaluate a chairside caries risk assessment protocol utilizing a caries prediction instrument, adenosine triphosphate (ATP) activity in dental plaque, mutans streptococci (MS) culture, and routine dental examination in five- to 10-year-old children at two regional Australian schools with high caries experience. Clinical indicators for future caries were assessed at baseline examination using a standardized prediction instrument. Plaque ATP activity was measured directly in relative light units (RLU) using a bioluminescence meter, and MS culture data were recorded. Each child's dentition was examined clinically and radiographically, and caries experience was recorded using enamel white spot lesions and decayed, missing, and filled surfaces for primary and permanent teeth indices. Univariate one-way analysis of variance between selected clinical indicators, ATP activity, MS count at baseline, and future new caries activity was performed, and a generalized linear model for prediction of new caries activity at 24 months was constructed. The results showed future new caries activity was significantly associated with the presence of visible cavitations, reduced saliva flow, and orthodontic appliances at baseline ($R(2) = 0.2$, $p < .001$), but baseline plaque adenosine triphosphate activity and mutans streptococci counts were not significantly associated with caries activity at 24 months.

Fazilat et al (2010) The authors conducted a cross-sectional study to demonstrate the use of adenosine triphosphate (ATP) driven bioluminescence as an innovative tool for the rapid chairside enumeration of oral bacteria (including plague streptococci) and assessment of oral hygiene and caries risk. Thirty-three pediatric patients (7- to 12-year-old males and females) were examined, and plague specimens, in addition to stimulated saliva, were collected from representative teeth within each quadrant. Oral specimens (n = 150 specimens) were assessed by plating on enriched and selective agars, to enumerate total bacteria and streptococci, and subjected to adenosine triphosphate- (ATP-) driven bioluminescence determinations using a luciferase-based assay system. Statistical correlations, linking ATP values to numbers of total bacteria, oral streptococci and mutans streptococci, yielded highly significant r values of 0.854, 0.840, and 0.796, respectively. The authors concluded that ATP measurements have a strong statistical association with bacterial number in plague and saliva specimens, including numbers for oral streptococci, and may be used as a potential assessment tool for oral hygiene and caries risk in children.

## Adjunctive Pre-Diagnostic Testing

In a 2021 Cochrane Database Systematic Review, Walsh et al. conducted an extensive literature search to evaluate the diagnostic accuracy of tests for the detection of oral cancer and oral potentially malignant disorders (OPMD) in patients that present with clinically evident and innocuous lesions. The also sought to estimate the relative accuracy of the different tests. Testing evaluated included vital staining, oral cytology, light-based detection and oral spectroscopy, and blood or saliva analysis (that test for the biomarkers in blood or saliva). Sixty-three studies of 7,942 lesions were included, however no eligible diagnostic accuracy studies evaluating blood or salivary sample analysis were identified. All studies used a reference test of biopsy and histopathological examination. The results showed the following:

- 20 studies of vital staining (rinsing and use of a dye impregnated swab) : sensitivity (low certainty evidence) 0.86; specificity (very low certainty evidence) 0.68.
- 20 studies of oral cytology (use of a brush and scraping): sensitivity (moderate certainty evidence) 0.90; specificity (moderate certainty evidence) 0.94.
- 23 studies of light- based devices (autofluorescence, tissue reflectance and electric scattering spectroscopy): sensitivity (low-certainty evidence) 0.87; (very low-certainty evidence) specificity 0.50.
- 9 studies of combined tests (vital staining with light-based detection, vital staining with brush cytology, and a staining method combining wheat germ agglutinin fluorescein isothiocyanate: sensitivity (very low certainty evidence) 0.78; (very low certainty evidence) specificity 0.71.

The authors concluded that none of the adjunctive tests can be recommended as a replacement for the currently used standard of a surgical biopsy and histological assessment. Oral cytology has relatively high sensitivity and specificity and offers the most potential. Combined adjunctive tests involving cytology, and salivary and blood biomarkers warrant further research.

Nagi et al. (2016). In a systematic review, the authors evaluated the effectiveness of devices that utilize the principles of chemiluminescence and tissue autofluorescence as adjuncts in the detection of oral squamous cell carcinoma (OSCC) and oral potentially malignant disorders (OPMD). Relevant articles were found in PubMed [MEDLINE] and Science direct and were limited to articles published in English or with an English abstract, from January 2005 to April 2014. Clinical trials utilized ViziLite, Microlux TM/DL and Visual Enhanced Light scope (VELscope) for early detection of OPMD and OSCC.

Twenty primary studies published satisfied the criteria for selection, and 10 utilized chemiluminescence and 10 tissue autofluorescence. Sensitivity of Vizilite for detecting OSCC and OPMD ranged from 77.1 % to 100% and specificity was low and ranged from 0% to 27.8%. Most showed that chemiluminescence increases the brightness and margins of oral mucosal white lesions and thus assists in identification of mucosal lesions not considered under conventional visual examination. However, it preferentially detects leukoplakia and may fail to spot red patches. Clinical trials demonstrated that sensitivity of VELscope in detecting malignancy and OPMD ranged from 22 % to 100 % and specificity ranged from 16 % to 100%. Most studies concluded that VELscope can help the experienced clinician to find oral precursor malignant lesions. But it could not differentiate between dysplasia and benign inflammatory conditions. The authors concluded that while both devices are simple, non-invasive test of the oral mucosa, they are best suited for clinicians with sufficient experience and training. More clinical trials in future should be conducted to establish optical imaging as an efficacious adjunct tool in early diagnosis of OSCC and OPMD.

Chainani-Wu et al. (2015) conducted a cross-sectional, observational study to evaluate the assessment methods that predict the presence of higher-risk oral premalignant lesions or higher-risk areas within lesions. Patients diagnosed with oral leukoplakia, erythroleukoplakia, or erythroplakia were selected and visual oral examination, ViziLite® examination, toluidine blue staining (TBlue®), and a biopsy were completed in a single clinic visit. There were 77 of 100 examined lesions in 43 patients biopsied. Sensitivity, specificity, and positive and negative predictive values were computed for visual examination, ViziLite, and TBlue using biopsy results as the gold standard. The results showed the sensitivity of TBlue in detecting high-risk lesions (carcinoma in situ or carcinoma) was 94 (71-100, $p < 0.0003$) and specificity 45 (32-58, $p < 0.53$), while for carcinoma, sensitivity was 100 (54-100, $p < 0.032$) and specificity 39 (28-52, $p < 0.097$). The results of ViziLite® testing either by itself or in combination with the information from toluidine blue testing revealed low sensitivity for the detection of high-risk lesions. The authors concluded that clinical examination of leukoplakia, erythroplakia, or erythroleukoplakia lesions combined with toluidine blue staining may aid in the identification of severe dysplasia (carcinoma in situ) or carcinoma. This may help in determining whether, when, and where (the site within a lesion) a biopsy should be taken.

Chhabra et al. (2015) conducted an extensive literature review of the various diagnostic modalities available at for the detection of squamous cell carcinomas and oral epithelial dysplasias. An advanced PUBMED search from 1972 to present was conducted and selected based on the desired criteria of being non-invasive, highly specific, and sensitive, economically viable, having a scope to be used for mass screening, easy to process, having low inter examiner variability and possibly not requiring high expertise to conduct and interpret the results. After reviewing various diagnostic modalities, the authors concluded that toluidine blue staining emerges as a valuable adjunct to incisional biopsy in detection of oral cancer but may not substitute it except in certain circumstances when its results are carefully correlated with the patient history and clinical characteristics of the mucosal disorder (considering the fact that incisional biopsy has been reported to cause dissemination of cancer cells in the circulation there by increasing the possibility of metastasis). The authors emphasize that toluidine blue is a screening modality and not a diagnostic procedure like biopsy and hence cannot replace a confirmatory biopsy as a whole, and that more detailed studies with large study samples are needed to investigate the reliability of toluidine blue staining and other screening methods in detection of oral cancer.

To evaluate the effectiveness of devices that utilize the principles of chemiluminescence and tissue autofluorescence as adjuncts in the detection of oral cancer and oral potentially malignant disorders (OPMDs), Rashid et al. (2015) conducted a systematic review of the published literature to evaluate the effectiveness of the ViziLite and ViziLite Plus with toluidine blue, MicroLux™/DL and the VELscope™. Twenty-five primary studies published between 2004 and 2013 satisfied the criteria for selection - 13 utilized chemiluminescence and 12 tissue autofluorescence, and several had utilized both study methods on the same population. The results showed chemiluminescence shows good sensitivity at detecting any OPMDs and oral cancer. However, it preferentially detects leukoplakia and may fail to spot red patches. The additive use of toluidine blue may improve specificity. Tissue autofluorescence is sensitive at detecting white, red, and white and red patches, and the area of fluorescence visualization loss (FVL) often extends beyond the clinically visible lesion. However, in addition to OPMDs, VELScope may detect erythematous lesions of benign inflammation resulting in false-positive test results. The authors concluded that there is limited evidence for the use of these devices as a primary diagnostic tool. Additionally, they may be better suited to use by specialists in clinics in which there is a higher prevalence of disease, and where experienced clinicians may better discriminate between benign and malignant lesions.

## Brush Biopsy

Datta et al. (2019) conducted a systematic review to assess the role of DNA-ICM (Image Cytometry) using samples from oral lesion brushing as an adjunct screening tool to differentiate high risk OPMLs from benign conditions and identify dysplasias at an increased risk of progression to malignancy. A total of 11 articles met the criteria. The studies were conducted in specialist hospitals or clinics based on community referrals for suspicious lesions in the mouth. None of the studies looked at the effectiveness of DNA-ICM as an adjunct screening tool in a community screening setting. None of the studies addressed whether DNA aneuploid OPMLs were more likely to show malignant transformation over time, and

none were longitudinal in design nor studied the lesions over time. The majority of the studies looked at the effectiveness of DNA-ICM in screening high risk OPMLs or differentiating malignant lesions from low risk or benign lesions. There was a wide variety of sensitivity and specificity when differentiating between high-risk and low-risk lesions which can be attributed to a lack of standardized DNA-ICM protocols, and definitions of high and low risk lesions and poor study designs. The authors concluded that due to significant limitations, there is poor evidence that these adjunctive tools are successful as an oral cancer screening tool. Studies with large sample sizes that follow established DNA quantification protocols for oral brushings are required before these adjuncts can be incorporated for routine use.

Kujan et al. (2019) conducted a study to investigate the feasibility of using oral liquid-based brush cytology (OLBC) coupled with immunocytochemistry as a minimally invasive approach to stratify the cancer risk in patients with oral leukoplakia. Fifty-five patients diagnosed with either oral leukoplakia (OLK) or oral squamous cell carcinomas (OSCC) were recruited. All patients underwent oral brush biopsy followed by surgical biopsy. 275 liquid-based cytology preparations were made. Pap-stained OLBC slides were assessed using the modified 2014 Bethesda Cytology system. The expression of CDK4, CDK6, cyclin D1, and Notch 1 was immunocytochemically analyzed and compared against the histopathological diagnosis. A combined index score of OLBC grading and protein expression was calculated. The results showed a significant association between the definitive histopathological diagnosis and the cytological interpretation ($p = 0.0005$). The index scores of CDK4, CDK6, and cyclin D1 were significantly associated with the development of disease from non-dysplastic epithelium to OSCC. No significant association was observed between the Notch 1 index score and disease stage. The diagnostic accuracy of OLBC showed the highest values of sensitivity, specificity, positive predictive value, negative predictive value, and accuracy: 84.6%, 70.4%, 73.3%, 82.6%, and 78.8%, respectively, compared with the cumulative protein index, CDK4/6 index, and the combined OLBC grading and CDK4/6 index. This study has also demonstrated the efficacy of the use of OLBC in the detection of OED and OSCC, and showed that the use of CDK4, CDK6, cyclin D1, and Notch 1 immunocytochemistry failed to improve the diagnostic accuracy of OLBC suggesting they are not useful in the early detection of OSCC.

H Alsarraf et al. (2018) conducted a systematic review to analyze the published evidence for the use of oral brush cytology for the early detection of oral cancer and oral potentially malignant disorders (OPMDs). The inclusion criteria involved studies assessing the utility of oral brush cytology on human tissues and its applications in the diagnosis, screening, or surveillance of oral cancer or OPMDs. 36 studies met the inclusion criteria, and a total of 4302 samples from OPMDs, oral squamous cell carcinoma, and healthy controls were investigated. Baby toothbrush, cytobrush, OralCDx®, and Orcellex® are the brushes that were used to obtain transepithelial mucosal samples for conventional and liquid-based cytology evaluation. Findings from this study indicate that meaningful evidence-based recommendations for the implementation of a minimally invasive technique to be utilized as an adjunctive tool for screening and early detection of oral cancer and OPMDs are complicated from the reported studies in the literature. The authors concluded there is need for well-designed clinical studies to assess the accuracy of oral brush cytology utilizing validated cytological assessment criteria for the diagnosis and prediction of OPMDs.

## Clinical Practice Guidelines

### *American Dental Association (ADA)*

In a 2020 policy on Public Health Emergencies, the ADA supported the temporary expansion of scope of practice for dentists who choose to participate for the following during declared local, state, or federal public health emergencies:

- Administering critical vaccines.
- Perform FDA-authorized diagnostic tests to screen patients for infectious diseases.
- Taking patient medical histories and triaging medical patients.
- Perform other ancillary medical procedures and activities, as requested by medical personnel, to expand the nation's surge capacity.

The 2017 Evidence-Based Clinical Practice Guideline for the Evaluation of Potentially Malignant Disorders in the Oral Cavity states that no available adjuncts demonstrated sufficient diagnostic test accuracy to support their routine use as triage tools during the evaluation of lesions in the oral cavity. For patients seeking care for suspicious lesions, immediate performance of a biopsy or referral to a specialist remains the single most important recommendation for clinical practice. In exceptional cases, when patients decline a biopsy or live in rural areas with limited access to care, the panel suggested that cytologic testing may be used to initiate the diagnostic process until a biopsy can be performed.

- The panel does not recommend autofluorescence, tissue reflectance, or vital staining adjuncts for the evaluation of potentially malignant disorders among adult patients with clinically evident, seemingly innocuous, or suspicious lesions.
- The panel does not recommend cytologic adjuncts for the evaluation of potentially malignant disorders among adult patients with clinically evident, seemingly innocuous, or suspicious lesions. Should a patient decline the clinician's

recommendation for performing a biopsy of the lesion or referral to a specialist, the clinician can use a cytologic adjunct to provide additional lesion assessment.
    - A positive or atypical cytologic test result reinforces the need for a biopsy or referral.
    - A negative cytologic test result indicates the need for periodic follow-up of the patient. If the clinician detects persistence or progression of the lesion, immediately performing a biopsy of the lesion or referral to a specialist is indicated.
- The panel does not recommend autofluorescence, tissue reflectance, or vital staining adjuncts for the evaluation of potentially malignant disorders among adult patients with clinically evident, seemingly innocuous, or suspicious lesions.
- The panel suggests that for adult patients with no clinically evident lesions or symptoms, no further action is necessary at that time.
- The panel does not recommend commercially available salivary adjuncts for the evaluation of potentially malignant disorders among adult patients with or without clinically evident, seemingly innocuous, or suspicious lesions and their use should be considered only in the context of research.

### *American Diabetes Association (ADA)*

American Diabetes Association Standards of Medical Care in Diabetes 2024:

- Because periodontal disease is associated with diabetes, the utility of chairside screening and referral to primary care as a means to improve the diagnosis of prediabetes and diabetes has been explored, with one study estimating that 30% of patients 30 years of age and older seen in general dental practices had dysglycemia. Further research is needed to demonstrate the feasibility, effectiveness, and cost-effectiveness of screening in this setting.
- Components of the comprehensive diabetes medical evaluation should include screening for the presence of dental diseases and referrals to a dentist for comprehensive dental and periodontal examination.

### *National Comprehensive Cancer Network (NCCN)*

In the 2024 practice guideline for head and neck cancers, the NCCN recommends biopsy for initial diagnosis and staging. Brush biopsies are not mentioned.

## U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

There are a number of caries detection devices that use fluorescence. Refer to the following website and search by product name or product code NBL: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm. (Accessed October 28, 2024)

For testing of microorganisms, according to the Office of In Vitro Diagnostics and Radiological Health (OIR), non-selective and differential culture media testing devices are considered to be Class I devices, and are exempted from the premarket notification requirement, and do not require FDA clearance before marketing in the U.S.; however, these manufacturers are required to register their establishment. Refer to the following website for additional information: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpcd/classification.cfm?id=jsh. (Accessed October 28, 2024)

Examples of adjunctive diagnostic devices used to detect mucosal abnormalities include Vizilite®, VELscope®, and Identafi®. Refer to the following website and search for additional products using Product Code EAZ: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm. (Accessed October 28, 2024)

Orcellex® and OralCDX® are examples of brush biopsy devices. These are Class I devices and exempt from premarket notification requirement and do not require FDA clearance before marketing in the U.S.; however, these manufacturers are required to register their establishment. Refer to the following website and search for Product Code GEE: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfRL/rl.cfm. (Accessed October 28, 2024)

## References

American Academy of Pediatric Dentistry Guideline on Caries-risk Assessment and Management for Infants, Children, and Adolescents Council on Clinical Affairs Committee. Adopted 2002. Revised 2022.

American Dental Association (ADA). Evaluation of Potentially Malignant Disorders of the Oral Cavity Clinical Practice Guideline. 2017.

American Dental Association (ADA). Public Health Emergencies. 2020. Available at: https://www.ada.org/about/governance/current-policies#publichealthemergencies. Accessed October 28, 2024.

American Dental Association (ADA) Glossary of Clinical and Administrative Terms.

American Diabetes Association Standards of Medical Care in Diabetes 2024.

American Diabetes Association Classification and Diagnosis of Diabetes. Standards of Medical Care in Diabetes. 2022.

Berman L, Rotstein I. Cohen's Pathways of the Pulp, 11th ed. St. Louis: Elsevier c2016. Chapter 1, Diagnosis; p. 2-32.

Chainani-Wu N, Madden E, Cox D, et al. Toluidine blue aids in detection of dysplasia and carcinoma in suspicious oral lesions. Oral Dis. 2015 Oct; 21(7):879-85.

Chhabra N, Chhabra S, Sapra N. Diagnostic modalities for squamous cell carcinoma: an extensive review of literature-considering toluidine blue as a useful adjunct. J Maxillofac Oral Surg. 2015 Jun;14(2):188-200.

Chinnasamy A, Moodie M. Prevalence of undiagnosed diabetes and prediabetes in the dental setting: A systematic review and meta-analysis. Int J Dent. 2020 Aug 25;2020:2964020.

Datta M, Laronde D, Palcic B, et al. The role of DNA image cytometry in screening oral potentially malignant lesions using brushings: A systematic review. Oral Oncol. 2019 Sep;96:51-59.

Eidson S, Shugars D. Sturdevant's Art and Science of Operative Dentistry, 6th ed. St. Louis: Mosby c2013. Chapter 3, Patient Assessment, Examination and Diagnosis, and Treatment Planning; p.104.

Fazilat S, Sauerwein R, McLeod J, et al. Application of adenosine triphosphate-driven bioluminescence for quantification of plaque bacteria and assessment of oral hygiene in children. Pediatr Dent. 2010 May-Jun; 32(3):195-204.

Genco RJ, Schifferle RE, Dunford RG, et al. Screening for diabetes mellitus in dental practices: a field trial. J Am Dent Assoc. 2014 Jan; 145(1):57-64.

Gilbert K, Joseph R, Vo A, et al. Children with severe early childhood caries: streptococci genetic strains within carious and white spot lesions. JOral Microbiol. 2014 Oct 29. Hallett KB, O'Rourke PK. Baseline dental plaque activity, mutans streptococci culture, and future caries experience in children. Pediatr Dent. 2013; 35(7):523-8.

H Alsarraf A, Kujan O, Farah CS. The utility of oral brush cytology in the early detection of oral cancer and oral potentially malignant disorders: A systematic review. J Oral Pathol Med. 2018 Feb;47(2):104-116.

Kujan O, Huang G, Ravindran A, et al. CDK4, CDK6, cyclin D1 and Notch1 immunocytochemical expression of oral brush liquid-based cytology for the diagnosis of oral leukoplakia and oral cancer. J Oral Pathol Med. 2019 Jun 7.

Lalla E, Cheng B, Kunzel C, et al. Six-month outcomes in dental patients identified with hyperglycaemia: a randomized clinical trial. J Clin Periodontol. 2015 Mar; 42(3):228-35.

Mataftsi M, Koukos G, Sakellari D. Prevalence of undiagnosed diabetes and pre-diabetes in chronic periodontitis patients assessed by an HbA1c chairside screening protocol. Clin Oral Investig. 2019 Apr 9.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology: Head and Neck Cancers. Version 5. 2024. October 24, 2024.

Nagi R, Reddy-Kantharaj YB, Rakesh N, et al. Efficacy of light based detection systems for early detection of oral cancer and oral potentially malignant disorders: Systematic review. Med Oral Patol Oral Cir Bucal. 2016 Jul 1; 21(4).D72.

Rashid A, Warnakulasuriya S. The use of light-based (optical) detection systems as adjuncts in the detection of oral cancer and oral potentially malignant disorders: a systematic review. J Oral Pathol Med. 2015 May; 44(5):307-28.

Rechmann P, Chaffee BW, Rechmann BMT, et al. Efficacy of an adenosine triphosphate meter for evaluating caries risk in clinical dental practice. J Am Dent Assoc. 2019 Oct;150(10):873-882.

Rethman MP, Carpenter W, Cohen EE, et al; American Dental Association Council on Scientific Affairs Expert Panel on Screening for Oral Squamous Cell Carcinomas. Evidence-based clinical recommendations regarding screening for oral squamous cell carcinomas. J Am Dent Assoc. 2010 May; 141(5):509-20.

Teeuw WJ, Kosho MX, Poland DC, et al. Periodontitis as a possible early sign of diabetes mellitus. BMJ Open Diabetes Res Care. 2017 Jan 19; 5(1):e000326.

U.S. Department of Health and Human Services. Fact Sheet: End of the COVID-19 Public Health Emergency. May 9, 2023. Available at: https://www.hhs.gov/about/news/2023/05/09/fact-sheet-end-of-the-covid-19-public-health-emergency.html#:~:text=At%20the%20end%20of%20the%20COVID%2D19%20PHE%20on%20May,19%20Vaccination%20Program%20Provider%20Agreement. Accessed October 28, 2024.

Walsh T, Macey R, Kerr AR, et al. Diagnostic tests for oral cancer and potentially malignant disorders in patients presenting with clinically evident lesions. Cochrane Database Syst Rev. 2021 Jul 20;7(7):CD010276.

World Health Organization. (2020). Naming the coronavirus disease (COVID-19) and the virus that causes it. https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/naming-the-coronavirus-disease-(covid-2019)-and-the-virus-that-causes-it. Accessed October 28, 2024.

# Policy History/Revision Information

| Date | Summary of Changes |
|---|---|
| 01/01/2025 | **Coverage Rationale**<br>• Removed list of examples of brush biopsies that are not indicated due to insufficient evidence of efficacy: Oral CDx®, BrushTest, and Orcellex<br>**Supporting Information**<br>• Updated *Description of Services*, *Clinical Evidence*, *FDA*, and *References* sections to reflect the most current information<br>• Archived previous policy version DCG040.09 |

# Instructions for Use

This Dental Clinical Policy provides assistance in interpreting UnitedHealthcare standard and Medicare Advantage dental plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard dental plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, please check the member specific benefit plan document and any applicable federal or state mandates. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Dental Clinical Policy is provided for informational purposes. It does not constitute medical advice.