Miscellaneous Diagnostic Procedures

Policy Number: DCP040.05
Effective Date: January 1, 2021

Instructions for Use

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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 (Not to Include Cytology or Biopsy Procedures)

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

Brush Biopsy

Brush biopsies (e.g., Oral CDx® The BrushTest, Orcellex) are not indicated due to insufficient evidence of efficacy. Pulp Vitality Tests

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 Testing

Antigen and antibody testing for public health related pathogens is out of scope for dental providers (*refer to the Description of Services section).

Exclusions

- Dental Services that are not Necessary
- Any Dental Procedure not directly associated with dental disease
- Procedures that are considered to be Experimental, Investigational or Unproven

Coverage Limitations

- Diagnostic casts are limited to 1 time per consecutive 24 months
- Pulp Vitality Tests are limited to 1 charge per visit, regardless of how many teeth are tested
- Adjunctive Pre-Diagnostic Test that aids in detection of mucosal abnormalities including premalignant and malignant lesions, not to include cytology or biopsy are limited to 1 time per consecutive 12 months

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.

Experimental, Investigational or Unproven Services: medical, dental, surgical, diagnostic, or other health care services, technologies, supplies, treatments, procedures, drug therapies or devices that, at the time we make a determination regarding Coverage in a particular case, is determined to be:

- Not approved by the U.S. Food and Drug Administration (FDA) to be lawfully marketed for the proposed use and not identified in the American Hospital Formulary Service or the United States Pharmacopoeia Dispensing Information as appropriate for the proposed use; or
- Subject to review and approval by any institutional review board for the proposed use; or
- The subject of an ongoing clinical trial that meets the definition of a Phase 1, 2 or 3 clinical trial set forth in the FDA regulations, regardless of whether the trial is actually subject to FDA oversight; or
- Not demonstrated through prevailing peer-reviewed professional literature to be safe and effective for treating or diagnosing the condition or illness for which its use is proposed; or
- Pharmacological regimens not accepted by the American Dental Association (ADA) Council on Dental Therapeutics.

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

Necessary: Dental Services and supplies which are determined by us through case-by-case assessments of care based on accepted dental practices to be appropriate; and

- Needed to meet your basic dental needs; and
- Rendered in the most cost-efficient manner and type of setting appropriate for the delivery of the Dental Service; and
- Consistent in type, frequency and duration of treatment with scientifically based guidelines of national clinical, research, or health care coverage organizations or governmental agencies that are accepted by us; and

- Consistent with the diagnosis of the condition; and
- Required for reasons other than the convenience of you or your Dental Provider; and
- Demonstrated through prevailing peer–reviewed dental literature to be either:
  - Safe and effective for treating or diagnosing the condition or sickness for which its use is proposed; or
  - Safe with promising efficacy:
    - For treating a life threatening dental disease or condition; and
    - In a clinically controlled research setting; and
    - Using a specific research protocol that meets standards equivalent to those defined by the National Institutes of Health.

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
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 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 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. On March 13, 2020 a national emergency was declared in the United States concerning the outbreak. This resulted in the cease of most elective medical and dental procedures for approximately two months. Individual States have set their own reopening schedules and phased reopening. The Centers for Disease Control and Prevention (CDC) issued the Guidance for Dental Settings, which recommends all patients be screened via the telephone for symptoms consistent with COVID 19 prior to all appointments. The guidance also recommends triaging, and encourages teledentistry when appropriate. The American Dental Association (ADA) released a document entitled "Guidance For Reopening During COVID-19", which echoes the CDC recommendations. *Antigen and antibody testing may only be performed by providers recognized by the United States Department of Health and Human Services (HHS) and individual State Dental Boards. As of this publication date, licensed pharmacists are the only providers outside of medical clinics that may order and administer COVID-19 tests. Guidelines may change as the situation is evolving rapidly.

Clinical Evidence

HbA1c Testing and Blood Glucose Level Testing

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

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.

Pellegrini et al (2009) Enamel decalcification is a common problem in orthodontics, and can lead to tooth decay. The objectives of this randomized clinical study were to enumerate and compare plaque bacteria surrounding 2 bracket types, self-ligating (SL) vs elastomeric ligating (E), and to determine whether adenosine triphosphate (ATP)-driven bioluminescence could be used for rapid assessment of bacterial load in plaque. 14 patients (ages 11-17 years) were bonded with SL and E brackets in 14 maxillary and 12 mandibular arches by using a split-mouth design. Recall visits were at 1 and 5 weeks after bonding. Plaque specimens were assayed for oral bacteria and subjected to ATP-driven bioluminescence determinations with a luciferin-based assay. In most patients, teeth bonded with SL attachments had fewer bacteria in plaque than did teeth bonded with E brackets. At 1 and 5 weeks after bonding, the means for SL vs E brackets were statistically lower for total bacteria and oral streptococci (P <0.05). ATP bioluminescence values were statistically correlated to the total oral bacteria and oral streptococci, with correlation coefficients of 0.895 and 0.843, respectively. SL appliances promote reduced retention of oral bacteria, and ATP bioluminescence might be a useful tool in the rapid quantification of bacterial load and the assessment of oral hygiene during orthodontic treatment.

Adjunctive Pre-Diagnostic Testing

Nagi et al. (20016). 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

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.

In a 2015 Cochrane Database Systematic review, Macey et al. sought to estimate the diagnostic accuracy of index tests for the detection of oral cancer and PMD of the lip and oral cavity, in people presenting with clinically evident lesions, as well as estimate the relative accuracy of the different index tests. 41 studies, with 4, 002 participants met the inclusion criteria of studies that reported the diagnostic test accuracy of the following index tests when used as an adjunct to conventional oral examination in detecting PMD or oral squamous cell carcinoma of the lip or oral cavity: vital staining, oral cytology, light-based detection and oral spectroscopy, blood or saliva analysis (which test for the presence of biomarkers in blood or saliva). For cytology, sensitivity was 0.91 (0.81 to 0.96) and specificity was 0.91 (0.81 to 0.95) with 12 studies included in the meta-analysis. The authors concluded that the overall quality of the included studies was poor, and none of the adjunctive tests can be recommended as a replacement for the currently used standard of a scalpel biopsy and histological assessment. Given the relatively high values of the summary estimates of sensitivity and specificity for cytology, this would appear to offer the most potential. Combined adjunctive tests involving cytology warrant further investigation.

Professional Societies

American Academy of Pediatric Dentistry (AAPD)

In the Guideline on Caries-Risk Assessment and Management for Infants, Children, and Adolescents, revised in 2014, the AAPD recommends the following:

- Due to a child's Mutans Streptococci (MS) levels and the age at which a child becomes colonized with cariogenic flora as being valuable in assessing risk, especially in preschool children, baseline testing on all children regardless of other risk factors/ risk level through the age of 5 is recommended.

American Dental Association (ADA)

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 (Lingen et al. 2017).

- 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 2020:

- 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.

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.

CariScreen is a device used for ATP bioluminescence testing of dental plaque. 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. See the following website for additional information: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpcd/classification.cfm?id=jsh. (Accessed August 26, 2020)

Also see the following consensus standard document. Quality Control for Commercially Prepared Microbiological Culture Media; Approved Standard - Third Edition. Available at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/detail.cfm?standard__identification_no=31793. (Accessed August 26, 2020)

Examples of adjunctive diagnostic devices used to detect mucosal abnormalities include Vizilite®, VELscope®, and Identafi®. Please see the following website and search for additional products using Product Code EAZ: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm. (Accessed August 26, 2020)

Orcellex®, a brush biopsy device, is a 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. See the following website and search for Product Code GEE: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfRL/rl.cfm. (Accessed August 26, 2020)

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Policy History/Revision Information

Date	Summary of Changes
03/15/2021	• Updated dental entity brand logo
01/01/2021	Template Update • Reformatted policy; transferred content to new template

Date	Summary of Changes

	Coverage Rationale
	In-Office HbA1c and Blood Glucose Level Tests
	• Revised language to state, 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
	Antigen and Antibody Testing
	• Added language stating antigen and antibody testing for public health related pathogens is out of scope for dental providers
	Definitions
	• Added definition of:
	  ○ Antibody
	  ○ Antigen
	Applicable Codes
	• Updated list of applicable CDT codes to reflect annual edits; added D0604 and D0605
	Supporting Information
	• Updated *Description of Services*, *Clinical Evidence*, *FDA*, and *References* sections to reflect the most current information
	• Archived previous policy version DCG040.04

Instructions for Use

This Dental Clinical Policy provides assistance in interpreting UnitedHealthcare standard dental benefit 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.