Agency for Healthcare Research and Quality
Advancing Excellence in Health Care

NATIONAL GUIDELINE CLEARINGHOUSE

General

Guideline Title

Evidence-based clinical practice guideline for the evaluation of potentially malignant disorders in the oral cavity: a report of the American Dental Association.

Bibliographic Source(s)

Lingen MW, Abt E, Agrawal N, Chaturvedi AK, Cohen E, D'Souza G, Gurenlian J, Kalmar JR, Kerr AR, Lambert PM, Patton LL, Sollecito TP, Truelove E, Tampi MP, Urquhart O, Banfield L, Carrasco-Labra A. Evidence-based clinical practice guideline for the evaluation of potentially malignant disorders in the oral cavity: a report of the American Dental Association. J Am Dent Assoc. 2017 Oct;148(10):712-27. [86 references] PubMed

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Rethman MP, Carpenter W, Cohen EE, Epstein J, Evans CA, Flaitz CM, Graham FJ, Hujoel PP, Kalmar JR, Koch WM, Lambert PM, Lingen MW, Oettmeier BW Jr, Patton LL, Perkins D, Reid BC, Sciubba JJ, Tomar SL, Wyatt AD Jr, Aravamudhan K, Frantsve-Hawley J, Cleveland JL, Meyer DM, American Dental Association Council on Scientific Affairs Expert Panel [trunc]. Evidence-based clinical recommendations regarding screening for oral squamous cell carcinomas. J Am Dent Assoc. 2010 May;141(5):509-20.

This guideline meets NGC's 2013 (revised) inclusion criteria.

NEATS Assessment

National Guideline Clearinghouse (NGC) has assessed this guideline's adherence to standards of trustworthiness, derived from the Institute of Medicine's report Clinical Practice Guidelines We Can Trust.

= Poor = Fair = Good = Very Good = Excellent

Assessment	Standard of Trustworthiness
YES	Disclosure of Guideline Funding Source

▮▮▮▮▯	Disclosure and Management of Financial Conflict of Interests
	Guideline Development Group Composition
YES	Multidisciplinary Group
YES	Methodologist Involvement
▮▮▮▮▮	Patient and Public Perspectives
	Use of a Systematic Review of Evidence
▮▮▮▮▮	Search Strategy
▮▮▮▮▮	Study Selection
▮▮▮▮▮	Synthesis of Evidence
	Evidence Foundations for and Rating Strength of Recommendations
▮▮▮▮▮	Grading the Quality or Strength of Evidence
▮▮▮▮▮	Benefits and Harms of Recommendations
▮▮▮▮▮	Evidence Summary Supporting Recommendations
▮▮▮▮▮	Rating the Strength of Recommendations
▮▮▮▮▮	Specific and Unambiguous Articulation of Recommendations
▮▮▮▮▯	External Review
▮▮▮▮▯	Updating

Recommendations

Major Recommendations

Definitions for the quality of the evidence (High, Moderate, Low, Very Low) and the strength of recommendations (Strong, Conditional) are provided at the end of the "Major Recommendations" field.

Summary of Good Practice Statements and Clinical Recommendations for the Evaluation of Potentially Malignant Disorders and Oral Squamous Cell Carcinomas in the Oral Cavity			
Clinical Question	**Recommendation**	**Quality of the Evidence**	**Strength of Recommendation**
No corresponding clinical question	Good practice statement: The panel suggests that clinicians* should obtain an updated medical, social, and dental history and perform an intraoral and extraoral conventional visual and tactile examination† in all adult patients.	No quality of evidence rating	No strength of recommendation assigned

Summary of Good Practice Statements and Clinical Recommendations for the Evaluation of Potentially Malignant Disorders and Oral Squamous Cell Carcinomas in the Oral Cavity

Clinical Question	Recommendation	Quality of the Evidence	Strength of Recommendation
Among adults with clinically evident, nonsuspicious lesions, or other symptoms,‡ should the panel recommend the use of adjuncts to identify potentially malignant or malignant disorders in the oral cavity?	Recommendation 1: The panel suggests that for adult patients with a clinically evident oral mucosal lesion with an unknown clinical diagnosis considered to be seemingly innocuous or nonsuspicious of malignancy, or other symptoms, clinicians should follow up periodically with the patient to determine the need for further evaluation. If the lesion has not resolved and the clinical diagnosis of a potentially malignant disorder cannot be ruled out, then clinicians should perform a biopsy of the lesion or refer the patient to a specialist.§	Low	Conditional
Among adults with clinically evident, suspicious lesions, or other symptoms, should the panel recommend adjuncts to identify potentially malignant or malignant disorders in the oral cavity?	Recommendation 2: The panel suggests that for adult patients with a clinically evident oral mucosal lesion considered to be suspicious of a potentially malignant or malignant disorder, or other symptoms, clinicians should perform a biopsy of the lesion or provide immediate referral to a specialist.	Low	Conditional
Among adults with clinically evident, nonsuspicious lesions, or other symptoms, should the panel recommend the use of adjuncts to identify potentially malignant or malignant disorders in the oral cavity? Among adults with clinically evident, suspicious lesions, or other symptoms, should the panel recommend adjuncts to identify potentially malignant or malignant disorders in the oral cavity?	Recommendation 3: 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.	Low	Conditional
Among adults with clinically evident, nonsuspicious lesions, or other symptoms, should the panel recommend the use of adjuncts to identify potentially malignant or malignant disorders in the oral cavity? Among adults with clinically evident, suspicious lesions, or other symptoms, should the panel recommend adjuncts to identify potentially malignant or malignant disorders in the oral cavity?	Recommendation 4: 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.	Low to very low	Conditional
Among apparently	Recommendation 5: The panel suggests that	Low	Conditional

Summary of Good Practice Statements and Clinical Recommendations for the Evaluation of Potentially Malignant Disorders and Oral Squamous Cell Carcinomas in the Oral Cavity			
Clinical Question	**Recommendation**	**Quality of the Evidence**	**Strength of Recommendation**
healthy adults with no clinically evident lesions, should the panel recommend the use of adjuncts to identify potentially malignant or malignant disorders in the oral cavity?	for adult patients with no clinically evident lesions or symptoms, no further action is necessary at that time		
Among apparently healthy adults with no clinically evident lesions, should the panel recommend the use of adjuncts to identify potentially malignant or malignant disorders in the oral cavity? Among adults with clinically evident, nonsuspicious lesions, or other symptoms, should the panel recommend the use of adjuncts to identify potentially malignant or malignant disorders in the oral cavity? Among adults with clinically evident, suspicious lesions, or other symptoms, should the panel recommend adjuncts to identify potentially malignant or malignant disorders in the oral cavity	Recommendation 6: 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.	Low	Conditional

**Clinician* refers to the target audience for this guideline, but only those trained to perform biopsies (that is, dentists) should do so.
†*Examination* refers to initial, routine, or emergency visits.
‡*Symptoms* could include globus sensation, unexplained ear or oropharyngeal pain, and hoarseness.
§*Specialist* refers to clinicians with advanced training in oral and maxillofacial surgery, oral and maxillofacial pathology, oral medicine, periodontology, and otolaryngology–head and neck surgery.

Definitions

Definition of Quality of or Certainty in the Evidence

Quality Level	Definition
High	The panel is very confident that the true effect lies close to that of the estimate of the effect.
Moderate	The panel is moderately confident in the effect estimate; the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low	Confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the effect.
Very Low	The panel has very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect.

Reproduced with permission from Balshem H, Helfand M, Schünemann HJ, et al. GRADE guidelines: the quality of evidence. J Clin

Epidemiol. 2011;64(4):401-406.

Quality Level	Definition

Definition of Strong and Conditional Recommendations and Implications for Stakeholders

Implications	Strong Recommendation	Conditional Recommendation
For Patients	Most people in this situation would want the recommended course of action, and only a small proportion would not. Formal decision aids are not likely to be needed to help people make decisions consistent with their values and preferences.	Most people in this situation would want the suggested course of action, but many would not.
For Clinicians	Most people should receive the intervention. Adherence to this recommendation according to the guideline could be used as a quality criterion or performance indicator.	Recognize that different choices will be appropriate for individual patients and that you must help each patient arrive at a management decision consistent with his or her values and preferences; decision aids may be useful in helping people to make decisions consistent with their values and preferences.
For Policy Makers	The recommendation can be adapted as policy in most situations.	Policy making will require substantial debate and involvement of various stakeholders.

Sources: Andrews J, Guyatt G, Oxman AD, et al. GRADE guidelines: 14. Going from evidence to recommendations—the significance and presentation of recommendations. J Clin Epidemiol. 2013;66(7):719-725; Andrews JC, Schünemann HJ, Oxman AD, et al. GRADE guidelines: 15. Going from evidence to recommendation—determinants of a recommendation's direction and strength. J Clin Epidemiol. 2013;66(7):726-735.

Clinical Algorithm(s)

An algorithm titled "Clinical pathway for the evaluation of potentially malignant disorders in the oral cavity" is provided in the original guideline document .

Scope

Disease/Condition(s)

Potentially malignant disorders (PMDs) and oral squamous cell carcinomas (OSCCs)

Note: Sarcomas or carcinomas of the lips, oropharynx, and salivary glands are not within the scope of this guideline.

Guideline Category

Diagnosis

Evaluation

Screening

Clinical Specialty

Dentistry

Oncology

Otolaryngology

Pathology

Intended Users

Advanced Practice Nurses

Allied Health Personnel

Dentists

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

To provide clinicians with updated evidence-based recommendations and suggest a clinical pathway regarding whether and when to use these adjuncts as triage tools for the evaluation of adult patients with no clinically evident lesions and clinically evident lesions, including potentially malignant disorders (PMDs), in the oral cavity

Target Population

Patients with no lesions, innocuous or nonsuspicious lesions, lesions suspected to be potentially malignant (that is, potentially malignant disorders [PMDs]), and malignant lesions (that is, oral squamous cell carcinoma [OSCC]) in the oral cavity

Interventions and Practices Considered

1. Medical, social, and dental history
2. Intraoral and extraoral conventional visual and tactile examination
3. Periodic follow up
4. Biopsy
5. Referral to a specialist
6. Use a cytologic adjunct to provide additional lesion assessment

Note: The following interventions were considered but not recommended: autofluorescence, tissue reflectance, or vital staining adjuncts; commercially available salivary adjuncts.

Major Outcomes Considered

- Oral cancer mortality
- Survival rate
- Unnecessary biopsy
- Quality of life
- All-cause mortality
- Incidence of oral cancer
- Anxiety and stress
- Costs

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

The systematic review report (see the "Availability of Companion Documents" field) follows the guidance of the Preferred Reporting Items for Systematic Reviews and Meta- Analyses statement and other methodological recommendations from the Cochrane Screening and Diagnostic Tests Methods Group.

Selection Criteria for the Studies in the Review

Type of Studies

The reviewers included cross-sectional and cohort diagnostic test accuracy (DTA) studies and randomized controlled trials (RCTs) in which the investigators assessed the effectiveness or accuracy of adjuncts. They excluded study designs such as case-control studies, case reports, case series, abstracts, and uncontrolled reports.

Type of Participants and Target Conditions

Studies eligible for inclusion involved adult patients (aged 18 years or older), ideally in the context of primary care settings, seeking care with or without clinically evident lesions in the oral cavity, encompassing the labial mucosae, buccal mucosae, gingival or alveolar ridge mucosae, tongue, floor of mouth, hard and soft palate, and retromolar trigone. If clinically evident, lesions could manifest as seemingly innocuous or nonsuspicious, suspicious, or seemingly malignant. The reviewers excluded studies involving patients seeking care for cancers of the lips, oropharynx, and salivary glands.

Index Tests and the Criterion Standard

Definitive diagnosis of potentially malignant disorders (PMDs) and oral squamous cell carcinoma (OSCC) requires using a criterion standard wherein the patient undergoes a biopsy of the lesion followed by a histopathologic assessment. Studies not specifying any criterion standard were ineligible for inclusion in this systematic review. Other tests, devices, techniques, or technologies intended to facilitate clinical decision making are index tests. The aforementioned adjuncts act as index tests in the context of this review and are used as triage tools in practice. Adjuncts can have either a positive (with suspicion of target condition) or negative (without suspicion of target condition) test result.

The reviewers defined several adjuncts of interest a priori and assessed them regarding their DTA and effectiveness when evaluating patients with:

- No clinically evident lesions in the oral cavity
- Clinically evident seemingly innocuous or nonsuspicious lesions in the oral cavity
- Clinically evident suspicious lesions or seemingly malignant lesions in the oral cavity

Adjuncts include the following:

- Cytologic testing (for example, OralCDx [OralScan Laboratories, Inc.], OralCyte [ClearCyte Diagnostics Inc.], ClearPrep OC [Resolution Biomedical])
- Autofluorescence (for example, VELscope [LED Dental], OralID [Forward Science]); tissue reflectance (for example, ViziLite Plus [DenMat Holdings, LLC], Microlux DL [AdDent Inc.])
- Vital staining (for example, toluidine blue)
- Salivary adjuncts (for example, OraRisk [Oral DNA Labs], SaliMark [PeriRx LLC], OraMark [OncAlert Labs], MOP genetic oral cancer screening [PCG Molecular], OraGenomics)
- Additional adjuncts of interest (for example, Identafi [StarDental])

The reviewers also included combinations of aforementioned adjuncts if 1 adjunct informed the use of the second adjunct. They reported results separately if the investigators used 2 index tests in a study

independently of each other. They excluded adjuncts not commercially available in the United States at the date of the search.

Types of Outcomes and Estimates

Patient-important outcomes are defined as "outcomes for which—even if it were the only outcome improved by the intervention—the patient would still consider receiving the intervention in face of some adverse events, costs, and burden." In the context of adjuncts, patients will prioritize outcomes such as morbidity and mortality and serious adverse events over other surrogate outcomes such as DTA estimates. The reviewers defined the following patient-important outcomes a priori and included all-cause mortality, OSCC mortality, survival, quality of life, unnecessary biopsy, costs, incidence of OSCC, and anxiety and stress. DTA estimates defined a priori included sensitivity, specificity, and positive and negative likelihood ratios. The reviewers used the proportion of true-positive, true-negative, false-positive, and false-negative results to calculate DTA estimates. The reviewers excluded studies when reporting made it impossible to create a contingency table.

Positivity Thresholds

As stated in the *Cochrane Handbook for Diagnostic Test Accuracy Reviews*, "binary test outcomes are defined on the basis of a threshold for test positivity and change if the threshold is altered." Whenever possible, the reviewers considered all levels of oral epithelial dysplasia (mild, moderate, and severe) assessed during biopsy or histopathologic assessment as positive for the target condition and absence of dysplasia assessed during biopsy or histopathologic assessment as negative for the target condition. For cytologic testing adjuncts, the reviewers grouped any atypical results with dysplastic results when possible and considered them positive for the target condition.

Using Preexisting Evidence

As a way to optimize the development of systematic reviews to inform American Dental Association (ADA) guidelines, the reviewers established a collaboration with the Cochrane Oral Health Group. The purpose of this collaboration was to increase efficiency in the use of secondary evidence for the development of clinical practice guidelines by using preexisting high-quality systematic reviews. In the event that no Cochrane reviews were available, they searched for non-Cochrane systematic reviews.

The eligible reviews had to meet 3 criteria. The first was being assessed as having moderate to high methodological quality. The second was being as current as possible. The third was meeting the selection criteria in relation to the type of study design, patient characteristics, index tests, criterion standard, and outcomes.

Identifying Relevant Systematic Reviews

The reviewers identified eligible systematic reviews through the collaboration with the Cochrane Oral Health Group. Members of the group suggested Cochrane reviews that potentially met the selection criteria. When no Cochrane reviews were available for a specific clinical question, they searched for non-Cochrane reviews by using the PubMed Clinical Queries tool and prioritized the most current ones (from 2010 to the present). To determine final eligibility, they used the Assessing the Methodological Quality of Systematic Reviews tool to assess their methodological quality.

Literature Search to Update Existing Reviews and Linked Evidence on Patient-important Outcomes

With the purpose of updating potentially eligible existing reviews, the reviewers searched MEDLINE via Ovid, EMBASE via Ovid, and the Cochrane Central Register of Controlled Trials. The reviewers included all study designs in the initial search. They also added economic analysis and patients' values and preferences (PVPs). After reviewing the results, they deemed it necessary to rerun the related Cochrane searches. The reviewers rebuilt the Cochrane searches for EMBASE, MEDLINE, and the Cochrane Central Register of Controlled Trials. They then restricted that language to RCTs, systematic reviews, and meta-analyses as a means of ensuring the update of the Cochrane review and to inform the patient-important outcomes (linked evidence) of interest. Given that literature related to salivary adjuncts was limited

within the bounds of the existing searches, they removed study design considerations to open up the possibilities of finding relevant language. The reviewers restricted the updated Cochrane searches from April 2013 (latest update by Cochrane) to December 2016. They ran the search on economic analysis and PVPs from inception to November 2016. The amended search for salivary adjuncts was run from April 2013 (latest update by Cochrane) to February 2017 (see Appendix 1 of the systematic review). The reviewers did not apply restrictions on language or publication status.

Selection of Primary Studies for Update of Systematic Reviews and Data Extraction

The reviewers conducted the study selection process in 3 phases. In the first phase, 2 reviewers independently reassessed eligibility of all included studies in the 2015 and 2013 Cochrane reviews. In the second phase, the same 2 reviewers independently screened titles and abstracts of retrieved references from the updated search strategy for both DTA studies and RCTs. In the third phase, reviewers independently screened the full text of all potentially eligible studies. They resolved any disagreements at full-text level via discussion and consensus. When consensus was elusive, a third reviewer arbitrated and decided final eligibility.

Number of Source Documents

Results of the Search

The reviewers identified 2 Cochrane reviews in which the investigators reported on diagnostic test accuracy (DTA) for adjuncts in patients both with and without clinically evident lesions developed by the Cochrane Oral Health Group. In addition, they identified 2 non-Cochrane reviews covering the use of salivary adjuncts.

From the 2015 Cochrane review, the reviewers identified 37 studies that were eligible. From the 2013 Cochrane review, no primary studies met the selection criteria. The other 2 non-Cochrane systematic reviews were published in 2016 and 2017 and covered salivary adjuncts for the early diagnosis of oral squamous cell carcinoma (OSCC), and no updating process was required.

During the updating process of the evidence from these reviews, the reviewers identified 7,534 references from the electronic databases. After eliminating duplicates, they screened the titles and abstracts of 6,708 citations. They selected 94 potentially eligible articles that were then screened using full texts. Of the 94 full-text articles, they selected 9 studies as part of the updating process and excluded the remaining 85 (eTable 3 in the systematic review [see the "Availability of Companion Documents" field]). This resulted in a total of 46 included studies (47 reports) (see Figure 1 in the systematic review). No studies on salivary adjuncts met the selection criteria, so they performed a comprehensive search to identify published systematic reviews.

During the process of identifying studies on patients' values and preferences (PVPs), the reviewers identified 2,616 citations and included 59 of those for full-text screening. Finally, 10 studies were eligible. Investigators in none of the studies reported on the relative importance of outcomes in the context of the use of adjuncts for the evaluation of potentially malignant disorders (PMDs).

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Definition of Quality of or Certainty in the Evidence

Quality Level	Definition
High	The panel is very confident that the true effect lies close to that of the estimate of the effect.
Moderate	The panel is moderately confident in the effect estimate; the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low	Confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the effect.
Very Low	The panel has very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect.
Reproduced with permission from Balshem H, Helfand M, Schünemann HJ, et al. GRADE guidelines: the quality of evidence. J Clin Epidemiol. 2011;64(4):401-406.	

Methods Used to Analyze the Evidence

Meta-Analysis of Randomized Controlled Trials

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Assessment of the Risk of Bias of Included Studies

Similar to methods used in other Cochrane systematic reviews on diagnostic test accuracy (DTA), the reviewers used a modified version of the quality assessment of diagnostic accuracy studies (QUADAS)-2 tool to assess the risk of bias and applicability of primary diagnostic accuracy studies included in the review. Two reviewers used the tool independently and in duplicate. They assessed the following domains in each study: patient selection, index test, criterion standard, and flow and timing. The reviewers assessed all domains in terms of the risk of bias by using signaling questions to assist in the judgments. They also assessed the first 3 domains in terms of their applicability. Other important considerations for the quality assessment included representativeness of the study sample, extent of verification bias, use of blinded methods for interpreting test results, and presence of missing data.

Data Synthesis and Meta-analysis

The reviewers recorded the number of true-positive, false-positive, true-negative, and false-negative results by using software (Review Manager, Version 5.3, Cochrane Collaboration). They recorded all new events at the lesion level to mirror the data presented in the 2015 Cochrane review. For each study, they displayed estimates of DTA, sensitivity, and specificity, along with their 95% confidence intervals (CIs), in coupled forest plots, as well as plotted in summary receiver operating characteristic curve space according to index test. The reviewers performed meta-analysis to obtain pooled estimates for sensitivity, specificity, and positive and negative likelihood ratios for each adjunct by using the bivariate approach (SAS, Version 9.4, SAS Institute). When too few studies were available for pooling by using the bivariate approach, they obtained the pooled estimate by combining their contingency tables for the associated comparison. The reviewers acknowledge that this method may have a tendency to create artificially narrower CIs. However, considering that this review is informing a clinical practice guideline, they prioritized the presentation of pooled estimates to facilitate decision making.

Assessment of the Quality of the Evidence

The reviewers assessed the quality of the evidence for all included outcomes by using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach with specification for the diagnostic test context. The GRADE approach provides a framework to assess the degree of confidence to

place in DTA and patient-important outcomes. In GRADE, crosssectional or cohort studies in patients with diagnostic uncertainty and a comparison with an appropriate criterion standard start as high-quality evidence (high certainty in the evidence). Certainty is reduced, however, when these studies have serious issues such as risk of bias or limitations in study design, indirectness, inconsistency, imprecision, or high probability of publication bias (see eTable 2 in the systematic review [see the "Availability of Companion Documents" field]). Such issues move the quality of the evidence from high to moderate, low, or very low certainty. The reviewers presented data in summary-of-findings tables created using software (GRADEpro Guideline Development Tool, McMaster University and Evidence Prime).

Data Extraction

Two reviewers independently and working in duplicate used a standardized form (Excel, Microsoft) to extract the data. They recorded the following data from each study: author's last name and year of publication, country, setting (primary, secondary, or tertiary care), population characteristics (age, sex, selection criteria, and clinical diagnosis of evident lesions), the number of patients included in the study, the number of lesions included in the analysis, index test and criterion standard characteristics, positivity thresholds, source of funding, financial and intellectual conflicts of interest, and diagnostic test accuracy (DTA) and patient-important outcomes. A third reviewer, who acted as arbiter, clarified any discrepancies between extractors. The reviewers made efforts to contact primary study authors whenever deemed necessary.

For a detailed description of the methods used to assess heterogeneity, publication bias, and the planned sensitivity analysis, see Appendix 2 of the systematic review.

Methods Used to Formulate the Recommendations

Expert Consensus (Consensus Development Conference)

Description of Methods Used to Formulate the Recommendations

Guideline Panel Configuration

The American Dental Association (ADA) Council on Scientific Affairs nominated and convened the 2017 expert panel for its clinical and subject matter expertise. The panel was configured carefully to include multidisciplinary viewpoints—general dentists, hygienists, oral medicine specialists, otolaryngologists, oncologists, oral and maxillofacial pathologists, oral and maxillofacial surgeons, and epidemiologists.

Moving from the Evidence to Decisions

The panel used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) evidence-to-decision framework to inform the process of formulating recommendations and to determine the strength of these statements. They assessed several domains during this process, including patient values and preferences, certainty in the evidence (quality of the evidence), balance between desirable and undesirable consequences (net effect), and resource use. In GRADE, the strength of recommendations can be either strong or conditional. Implications for stakeholders such as patients, clinicians, and policy makers vary between strong and conditional recommendations (see the "Rating Scheme for the Strength of the Recommendations" field).

Process of Formulating Recommendations

The panel formulated the clinical questions, outcomes of interest, and final recommendations contained in this article during 2 in-person expert panel meetings held in September 2016 and January 2017. Methodologists from the ADA Center for Evidence-Based Dentistry facilitated both meetings. The panel used guidance from the GRADE approach, deliberation, and consensus during implementation of the evidence-to-decision framework. If consensus was elusive, they presented all possible options with assessments for a panel vote.

Rating Scheme for the Strength of the Recommendations

Definition of Strong and Conditional Recommendations and Implications for Stakeholders

Implications	Strong Recommendation	Conditional Recommendation
For Patients	Most people in this situation would want the recommended course of action, and only a small proportion would not. Formal decision aids are not likely to be needed to help people make decisions consistent with their values and preferences.	Most people in this situation would want the suggested course of action, but many would not.
For Clinicians	Most people should receive the intervention. Adherence to this recommendation according to the guideline could be used as a quality criterion or performance indicator.	Recognize that different choices will be appropriate for individual patients and that you must help each patient arrive at a management decision consistent with his or her values and preferences; decision aids may be useful in helping people to make decisions consistent with their values and preferences.
For Policy Makers	The recommendation can be adapted as policy in most situations.	Policy making will require substantial debate and involvement of various stakeholders.
Sources: Andrews J, Guyatt G, Oxman AD, et al. GRADE guidelines: 14. Going from evidence to recommendations—the significance and presentation of recommendations. J Clin Epidemiol. 2013;66(7):719-725; Andrews JC, Schünemann HJ, Oxman AD, et al. GRADE guidelines: 15. Going from evidence to recommendation—determinants of a recommendation's direction and strength. J Clin Epidemiol. 2013;66(7):726-735.		

Cost Analysis

The reviewers ran the search on economic analysis and patient values and perspectives (PVPs) from inception to November 2016.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

Stakeholder and Public Feedback

The panel contacted internal American Dental Association (ADA) and external stakeholders on 2 occasions: at the beginning of the guideline development process to obtain feedback on the definition of the scope and purpose, target audience and population, clinical questions, adjuncts, and outcomes for decision making and after formulating recommendations to obtain input about the clarity and appropriateness of the recommendation statements and the assessment of the quality of the evidence and strength of the recommendations. In addition, they posted a draft of the guideline's scope and purpose, target audience and users, and recommendation statements on the ADA's Web site with the purpose of obtaining comments from the general public. The panel and methodological team logged and considered these comments and incorporated them when writing this article.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- Patients with true-positive test results will be identified correctly as having a potentially malignant or malignant disorder, and timely referral to a specialist or a biopsy will be performed.
- Patients with true-negative test results will receive reassurance that they do not have a potentially malignant or malignant disorder.

Potential Harms

- For patients with false-negative test results, an appropriate diagnosis would be missed, worsening the prognosis of the disease.
- Patients with false-positive test results would be identified incorrectly as having a potentially malignant or malignant disorder and would undergo additional unnecessary testing and a biopsy.

Qualifying Statements

Qualifying Statements

When applying these recommendations in primary care settings such as dental offices or clinics, one must consider that investigators in much of the existing literature describe the use of adjuncts in secondary and tertiary care settings such as specialty clinics or hospitals. This is an important consideration because investigators have not studied the diagnostic test accuracy of the adjuncts thoroughly in primary care settings, where the prevalence of disease could modify the diagnostic test accuracy of these adjuncts. Another point to consider is that clinicians in secondary and tertiary care settings are advanced in relevant experience and skill and can evaluate and triage lesions more appropriately by using conventional visual and tactile examination (CVTE) alone than can primary care clinicians. Furthermore, referral to a specialist for a biopsy (clinicians with advanced training in oral and maxillofacial surgery, oral and maxillofacial pathology, oral medicine, periodontology, and otolaryngology–head and neck surgery) is indicated when clinicians are not trained or skilled adequately to perform a biopsy.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Patient Resources

Pocket Guide/Reference Cards

Resources

Staff Training/Competency Material

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

Lingen MW, Abt E, Agrawal N, Chaturvedi AK, Cohen E, D'Souza G, Gurenlian J, Kalmar JR, Kerr AR, Lambert PM, Patton LL, Sollecito TP, Truelove E, Tampi MP, Urquhart O, Banfield L, Carrasco-Labra A. Evidence-based clinical practice guideline for the evaluation of potentially malignant disorders in the oral cavity: a report of the American Dental Association. J Am Dent Assoc. 2017 Oct;148(10):712-27. [86 references] PubMed

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2017 Oct

Guideline Developer(s)

American Dental Association - Professional Association

Source(s) of Funding

The American Dental Association (ADA) Council on Scientific Affairs commissioned this work.

Guideline Committee

American Dental Association (ADA) Council on Scientific Affairs and the Center for Evidence-Based Dentistry Expert Panel

Composition of Group That Authored the Guideline

Panel Members: Mark W. Lingen, DDS, PhD, FRCPath; Elliot Abt, DDS, MS, MSc; Nishant Agrawal, MD; Anil K. Chaturvedi, PhD; Ezra Cohen, MD, FRCPSC; Gypsyamber D'Souza, PhD; JoAnn Gurenlian, RDH, PhD; John R. Kalmar, DMD, PhD; Alexander R. Kerr, DDS, MSD; Paul M. Lambert, DDS; Lauren L. Patton, DDS; Thomas P. Sollecito, DMD, FDS, RCS; Edmond Truelove, DDS, MSD; Malavika P. Tampi, MPH; Olivia Urquhart, MPH; Laura Banfield, MLIS, MHS; Alonso Carrasco-Labra, DDS, MSc

Financial Disclosures/Conflicts of Interest

Conflict of Interest Management

Whenever possible, the panel attempted to avoid involving expert panelists with extensive conflicts of interest. All panel members who initially were invited were asked to complete a form providing information about any potential financial and intellectual conflicts of interest within the past 2 years. For the sake of transparency, they summarized and presented all potential conflicts to the entire panel at the beginning of both in-person meetings. As part of the methodology, they planned that any member of the panel considered to be highly conflicted would need to refrain from participating in the formulation of recommendations for which they identified conflicts.

Disclosures

Dr. Lingen has received research funding from the National Institute of Dental and Craniofacial Research (NIDCR) and the National Cancer Institute (NCI). In addition, he is the editor-in-chief of *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology* and the vice president of the American Academy of Oral and Maxillofacial Pathology. Dr. Agrawal has received funds from the National Institutes of Health (NIH) to conduct research focused on head and neck cancer genetics and tumor DNA in the saliva and plasma of patients with head and neck cancer. He is also on the editorial board of *Scientific Reports*. Dr. Chaturvedi has received funds from the Intramural Program of the NCI to conduct research focused on the natural history of oral cancer precursor lesions. He is an employee at the NCI NIH, and authorship in this guideline is considered his opinion and not that of the NCI NIH. Dr. Cohen is a consultant to AstraZeneca, Bristol-Myers Squibb, Human Longevity, Merck, Merck Serono, and Pfizer. Dr. D'Souza has received funds from the NIDCR. Dr. Kalmar has received funds from The Ohio State University to conduct research on determining surgical margins by using VELscope (LED Medical Diagnostics). Dr. Kerr has received funds from the NIDCR to conduct research focused on increasing oral cancer screening by dentists. Dr. Patton is a coeditor of the second edition of *The ADA Practical Guide to Patients With Medical Conditions*. She also has received funds from the NIDCR to conduct research focused on a clinical registry of dental outcomes in patients with head and neck cancer. In addition, she is the oral medicine section editor of *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology*, and she is vice president of the American Academy of Oral Medicine. Dr. Sollecito is the director and treasurer of the American Board of Oral Medicine, a site visitor for the Commission on Dental Accreditation, and a regional director for the Royal College of Surgeons Edinburgh. He also has received funds from the NIDCR to conduct research focused on a clinical registry of dental outcomes in patients with head and neck cancer. Ms. Tampi, Mrs. Urquhart, and Dr. Carrasco-Labra have no disclosures to report.

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Rethman MP, Carpenter W, Cohen EE, Epstein J, Evans CA, Flaitz CM, Graham FJ, Hujoel PP, Kalmar JR, Koch WM, Lambert PM, Lingen MW, Oettmeier BW Jr, Patton

LL, Perkins D, Reid BC, Sciubba JJ, Tomar SL, Wyatt AD Jr, Aravamudhan K, Frantsve-Hawley J, Cleveland JL, Meyer DM, American Dental Association Council on Scientific Affairs Expert Panel [trunc]. Evidence-based clinical recommendations regarding screening for oral squamous cell carcinomas. J Am Dent Assoc. 2010 May;141(5):509-20.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the Journal of the American Dental Association Web site .

Availability of Companion Documents

The following are available:

Lingen MW, Tampi MP, Urquhart O, Abt E, Agrawal N, Chaturvedi AK, Cohen E, D'Souza G, Gurenlian J, Kalmar JR, Kerr AR, Lambert PM, Patton LL, Sollecito TP, Truelove E, Banfield L, Carrasco-Labra A. Adjuncts for the evaluation of potentially malignant disorders in the oral cavity: diagnostic test accuracy systematic review and meta-analysis-a report of the American Dental Association. J Am Dent Assoc. 2017 Nov;148(11):797-813.e52. Available from the Journal of the American Dental Association Web site .

Gualtero DF, Suarez Castillo A. Biomarkers in saliva for the detection of oral squamous cell carcinoma and their potential use for early diagnosis: a systematic review. Acta Odontol Scand. 2016;74(3):170-7. Available to subscribers from the Acta Odontological Scandinavica Web site .

Stuani VT, Rubira CM, Sant'Ana AC, Santos PS. Salivary biomarkers as tools for oral squamous cell carcinoma diagnosis: a systematic review. Head Neck. 2017 Apr;39(4):797-811. Available to subscribers from the Head & Neck Web site .

Evidence-based clinical practice guideline for the evaluation of potentially malignant disorders in the oral cavity: a report of the American Dental Association. Chairside guide. Chicago (IL): American Dental Association; 2017. 2 p. Available from the American Dental Association (ADA) Center for Evidence-based Dentistry (EBD) Web site .

Evidence-based clinical practice guideline for the evaluation of potentially malignant disorders in the oral cavity: a report of the American Dental Association. Instructional video. Chicago (IL): American Dental Association; 2017. Available from the ADA Center for EBD Web site .

A continuing education activity available from the Journal of the American Dental Association Web site .

Patient Resources

The following is available:

Mark AM. Oral cancer: What to do if something unusual shows up. J Am Dent Assoc. 2017 Oct;148(10):780. Available from the Journal of the American Dental Association Web site .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

This NGC summary was completed by ECRI Institute on January 7, 2011. The information was verified by the guideline developer on February 14, 2011. This summary was updated by ECRI Institute on March 20, 2018. The information was verified by the guideline developer on April 11, 2018.

This NEATS assessment was completed by ECRI Institute on March 15, 2018. The information was verified by the guideline developer on April 11, 2018.

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