



CMS Measure ID/CMS QCDR ID: CAP 36

Measure Title: p16 Immunohistochemistry Reporting for Human Papillomavirus in Patients with Oropharyngeal Squamous Cell Carcinoma (OPSCC)

Measure Specifications

<b>Measure Description</b>	Percentage of surgical pathology reports for invasive oropharyngeal squamous cell carcinoma (OPSCC) with quantitative p16 immunohistochemistry (IHC) using a $\geq 70\%$ nuclear and cytoplasmic staining cutoff performed as a surrogate for HR-HPV status
<b>Denominator Statement</b>	<p>All surgical pathology reports with a diagnosis of invasive OPSCC.</p> <p>CPT®: 88305, 88309</p> <p><b>AND</b></p> <p>ICD10:</p> <ul style="list-style-type: none"> <li>• C01: Malignant neoplasm of base of tongue</li> <li>• C05.1: Malignant neoplasm of soft palate</li> <li>• C09.0: Malignant neoplasm of tonsillar fossa</li> <li>• C09.1: Malignant neoplasm of tonsillar pillar (anterior) (posterior)</li> <li>• C09.8: Malignant neoplasm of overlapping sites of tonsil</li> <li>• C09.9: Malignant neoplasm of tonsil, unspecified</li> <li>• C10.0: Malignant neoplasm of vallecula</li> <li>• C10.1: Malignant neoplasm of anterior surface of epiglottis</li> <li>• C10.2: Malignant neoplasm of lateral wall of oropharynx</li> <li>• C10.3: Malignant neoplasm of posterior wall of oropharynx</li> <li>• C10.4: Malignant neoplasm of branchial cleft</li> <li>• C10.8: Malignant neoplasm of overlapping sites of oropharynx</li> <li>• C10.9: Malignant neoplasm of oropharynx, unspecified</li> <li>• C14.0: Malignant neoplasm of pharynx, unspecified</li> <li>• C14.2: Malignant neoplasm of Waldeyer's ring</li> <li>• C14.8: Malignant neoplasm of overlapping sites of lip, oral cavity and pharynx</li> <li>• C77.0: Secondary and unspecified malignant neoplasm of lymph nodes of head, face and neck</li> </ul>
<b>Denominator Exclusions</b>	<p>Non-squamous cell carcinoma of the oropharynx</p> <p>Non-oropharyngeal primary tumors of the head and neck</p>
<b>Denominator Exceptions</b>	Documentation of reason(s) p16 IHC testing was not performed (e.g., payor-related limitations, patients who have declined testing, patients receiving hospice)
<b>Numerator Statement</b>	Pathology reports containing documentation of p16 IHC performed (currently or previously) as a surrogate marker for presence of HR-HPV AND where p16 status is described using the $\geq 70\%$ nuclear and cytoplasmic staining cutoff*



	*p16 quantitation: p16 IHC is considered positive and a surrogate for the presence of HR-HPV when the tumor shows ≥70% nuclear and cytoplasmic immunoreactivity with moderate to strong intensity.
<b>Numerator Exclusions</b>	None
<b>Guidance</b>	<p><u>Denominator Guidance</u> Includes invasive OPSCC reports for specimens from primary tumors (tonsils, soft palate, or base of tongue (posterior to circumvallate papillae) and lateral and posterior pharyngeal walls) OR metastatic squamous cell carcinoma of unknown primary in a cervical upper or mid jugular chain lymph node. Secondary malignant neoplasms elsewhere in the body are not considered.</p> <p><u>Numerator Guidance</u> Quantitative p16 IHC results may include:</p> <ul style="list-style-type: none"> <li>• p16 IHC positive (≥70% nuclear and cytoplasmic moderate to strong staining)</li> <li>• p16 IHC negative (&lt; 70% nuclear and cytoplasmic moderate to strong staining)</li> <li>• p16 previously performed (includes recurrent tumors where testing was performed on the primary tumor)</li> <li>• p16 cannot be determined</li> </ul> <p>The pathology report must include an interpretation statement (as noted above) by the reporting pathologist; a link to a report from a reference lab or statement about ordering testing is not sufficient</p>
<b>Measure Information</b>	
<b>NQS Domain</b>	Communication and Care Coordination
<b>Meaningful Measures Area(s)</b>	Transfer of Health Information and Interoperability
<b>Meaningful Measure Rationale</b>	<p>Human papillomavirus (HPV) is a major cause of oropharyngeal squamous cell carcinoma (OPSCC) and has contributed to its increased incidence (1). HPV-positive OPSCC differs from HPV-negative OPSCC related to other risk factors including alcohol and tobacco use and has an improved response to treatment and better prognosis (2).</p> <p>Therefore, it is crucial to determine the HPV status of squamous cell carcinomas of the oropharynx, as treating clinicians utilize this information when developing a treatment plan for patients, which may include less aggressive treatment modalities. In the clinical setting, p16 IHC is an approach used to reliably diagnose HPV-induced OPSCC.</p> <p>The p16 test is considered to best stratify patient survival outcomes while also being practical and inexpensive (3). Furthermore, data suggest that the correlation between HPV positivity and p16 overexpression is highest when the ≥70% staining for p16 overexpression is applied (4).</p>



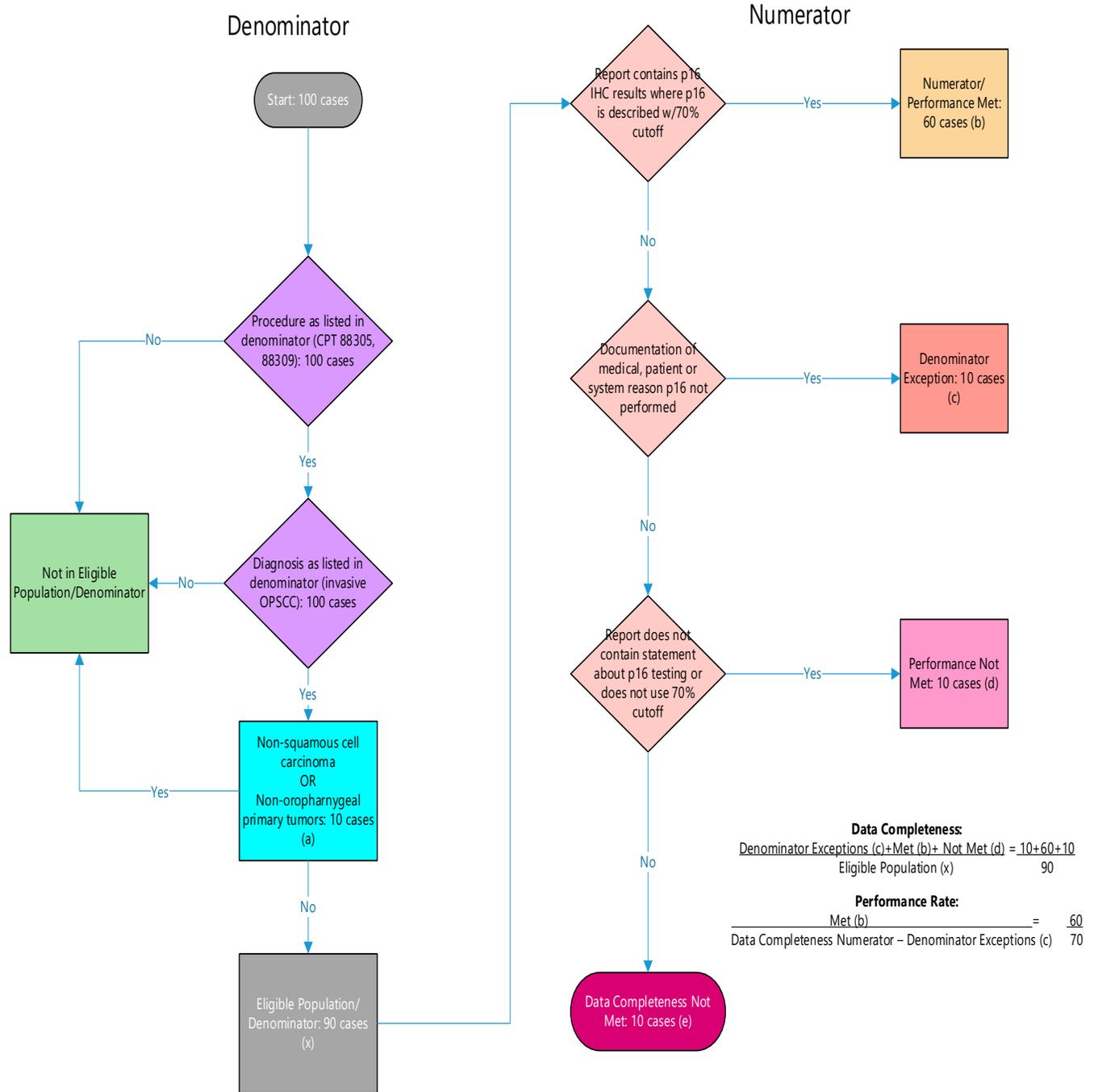
	<ol style="list-style-type: none"> <li>1. Chaturvedi AK, Engels EA, Pfeiffer RM, et al. Human papillomavirus and rising oropharyngeal cancer incidence in the United States. <i>J Clin Oncol.</i> 2011;29(32):4294–4301.</li> <li>2. Wang MB, Liu IY, Gornbein JA, Nguyen CT. HPV-positive oropharyngeal carcinoma: a systematic review of treatment and prognosis. <i>Otolaryngol Head Neck Surg.</i> 2015. Nov;153(5):758-69.</li> <li>3. Lewis JS Jr, Beadle B, Bishop JA, Chemock RD, Colasacco C, Lacchetti C, et al. Human papillomavirus testing in head and neck carcinomas: guideline from the College of American Pathologists. <i>Arch Pathol Lab Med.</i> 2018;142:559–597.</li> <li>4. Grønhøj Larsen C, Gyldenløve M, Jensen DH, Therkildsen MH, Kiss K, Norrild B, Konge L, von Buchwald C. Correlation between human papillomavirus and p16 overexpression in oropharyngeal tumours: a systematic review. <i>Br J Cancer.</i> 2014. Mar 18;110(6):1587-94.</li> </ol>
<b>Measure Type</b>	Process
<b>Data Source</b>	Laboratory Information Systems; pathology reports
<b>Summary of Performance Gap Evidence</b>	<p>In 2019, one practice reported this measure to CMS via the Pathologists Quality Registry. The performance rate of that practice was 85.71%. This was using a previous version of the measure, but the overall quality action was the same.</p> <p>In a meta-review of 39 studies, 17 studies (n=1684) used a minimum of 5-69% staining to indicated positive results, 7 studies (n=764) used &gt;70% and fifteen studies (n=1478) referred to a verbal definition (1). Therefore only 7 studies (17.9%) were in compliance with the guideline. A separate meta-analysis found that of 22 papers published between 2010 and 2017, all of which reported IHC staining, only 11 (50%) used the 70% staining cutoff to indicate positive results (2).</p> <ol style="list-style-type: none"> <li>1. C Grønhøj Larsen, M Gyldenløve, D H Jensen, M H Therkildsen, K Kiss, B Norrild, L Konge &amp; C von Buchwald. (2014) Correlation between human papillomavirus and p16 overexpression in oropharyngeal tumours: a systematic review. <i>British Journal of Cancer</i> 110:1587–1594</li> <li>2. Prigge, E. , Arbyn, M. , von Knebel Doeberitz, M. and Reuschenbach, M. (2017), Diagnostic accuracy of p16INK4a immunohistochemistry in oropharyngeal squamous cell carcinomas: A systematic review and meta-analysis. <i>Int. J. Cancer</i>, 140: 1186-1198.</li> </ol>
<b>Measure Owner</b>	College of American Pathologists
<b>NQF ID</b>	N/A
<b>Number of Performance Rates</b>	1



<b>Overall Performance Rate</b>	1 <sup>st</sup> Performance Rate
<b>High-priority</b>	Yes
<b>Improvement Notation</b>	Inverse Measure: No <b>Proportional Measure: Yes (Higher score indicates better quality)</b> Continuous Variable Measure: No Ratio Measure: No Risk-adjusted: No
<b>Care Setting and Specialty</b>	Care Setting: Other—Laboratories; Telehealth not applicable Specialty: Pathology
<b>Current Clinical Guideline the Measure is Derived From</b>	<p>Pathologists should perform high-risk human papillomavirus (HR-HPV) testing on all patients with newly diagnosed oropharyngeal squamous cell carcinoma (OPSCC). This testing may be performed on the primary tumor or on a regional lymph node metastasis when the clinical findings are consistent with an oropharyngeal primary (Strong Recommendation) (1).</p> <p>For oropharyngeal tissue specimens (i.e., noncytology), pathologists should perform HR HPV testing by surrogate marker p16 immunohistochemistry (IHC). Additional HPV-specific testing may be done at the discretion of the pathologist and/or treating clinician, or in the context of a clinical trial (Recommendation) (1).</p> <p>Pathologists should report p16 IHC positivity as a surrogate for HR-HPV in tissue specimens (i.e., noncytology) when there is at least 70% nuclear and cytoplasmic expression with at least moderate to strong intensity (Expert Consensus Opinion) (1).</p> <p>Tumor human papillomavirus (HPV) testing by p16 immunohistochemistry (IHC) required as part of the workup for cancer of the oropharynx (Category 2A) (2).</p> <ol style="list-style-type: none"> <li>1. Lewis JS Jr, Beadle B, Bishop JA, Chemock RD, Colasacco C, Lacchetti C, et al. Human papillomavirus testing in head and neck carcinomas: guideline from the College of American Pathologists. Arch Pathol Lab Med. 2018;142:559–597.</li> <li>2. Pfister DG, Spencer S, Adelstein D, Adkins D, Brizel DM, Burtness B, et al. NCCN clinical practice guidelines in oncology: head and neck cancers, version 2.2018. National Comprehensive Cancer Network. Available at <a href="https://www.nccn.org/professionals/physician_gls/recently_updated.aspx">https://www.nccn.org/professionals/physician_gls/recently_updated.aspx</a></li> </ol>



Measure Flow



**Data Completeness:**  

$$\frac{\text{Denominator Exceptions (c)} + \text{Met (b)} + \text{Not Met (d)}}{\text{Eligible Population (x)}} = \frac{10 + 60 + 10}{90}$$

**Performance Rate:**  

$$\frac{\text{Met (b)}}{\text{Data Completeness Numerator} - \text{Denominator Exceptions (c)}} = \frac{60}{70}$$