# Adjunctive Techniques for Screening and Surveillance of Barrett Esophagus and Esophageal Dysplasia

**Policy #** 00757
Original Effective Date: 11/08/2021
Current Effective Date: 11/13/2023

*Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.*

*Note: Endoscopic Radiofrequency Ablation or Cryoablation for Barrett Esophagus is addressed separately in medical policy 00261.*

## Services Are Considered Investigational

*Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.*

Based on review of available data, the Company considers wide-area transepithelial sampling with three-dimensional computer-assisted analysis (WATS3D) and other esophageal brush biopsy tests (e.g., EsoGuard), for all indications, including but not limited to the screening and surveillance of Barrett esophagus (BE) and esophageal dysplasia to be **investigational.***

## Background/Overview

### Barrett Esophagus

Barrett esophagus (BE) is a condition in which the squamous epithelium that normally lines the esophagus is replaced by specialized columnar-type epithelium known as intestinal metaplasia in response to irritation and injury caused by gastroesophageal reflux disease (GERD). Barrett esophagus occurs in the distal esophagus. It may involve any length of the esophagus, be focal or circumferential, and is visualized on endoscopy with a different color than background squamous mucosa. Confirmation of BE requires a biopsy of the columnar epithelium and microscopic identification of intestinal metaplasia. The prevalence of BE in the United States is estimated at 5.6%. Risk factors associated with the development of BE include GERD, male gender, central obesity, and age over 50 years. The diagnosis of GERD is associated with a 10% to 15% risk of BE. However, a population-based analysis from Sweden observed that 40% of the study cohort with esophageal cancer reported no prior history of GERD symptoms.

***Cancer Risk and Management***

Intestinal metaplasia is a precursor to esophageal adenocarcinoma, and patients with BE are at a 40-fold increased risk for developing this disease compared to the general population.

However, there are few data to guide recommendations about management and surveillance, and many issues are controversial. Guidelines from the American College of Gastroenterology (ACG) and a consensus statement from an international group of experts (Benign Barrett's and CAncer Taskforce) on the management of BE are published. The ACG recommendations for surveillance are stratified by the presence and grade of dysplasia.

When no dysplasia is detected, ACG has reported the estimated risk of progression to cancer ranges from 0.2% to 0.5% per year and endoscopic surveillance every 3 to 5 years is recommended. For low-grade dysplasia, the estimated risk of progression is 0.7% per year, and endoscopic therapy is preferred; however, endoscopic surveillance every 12 months is considered an acceptable alternative. It is recommended that both options are discussed with the patient. Precise estimates of cancer risk are not available for individuals with low-grade dysplasia due to large disparities among studies on its natural history. Interobserver variability in the diagnosis of low-grade dysplasia with standard biopsy may be responsible, with expert pathologists commonly downgrading initial diagnoses made by community pathologists.

The Benign Barrett's and CAncer Taskforce consensus group did not endorse routine surveillance for people without dysplasia and was unable to agree on surveillance intervals for low-grade dysplasia.

For high-grade dysplasia, the estimated risk of progression is about 7% per year, and ACG has recommended endoscopic eradication therapy, with the type of procedure dependent on patient age and life expectancy, comorbidities, the extent of dysplasia, local expertise in surgery and endoscopy, and patient preference. Approximately 40% of patients with high-grade dysplasia on biopsy are found to have associated carcinoma in the resection specimen.

For patients who are indefinite for dysplasia, a repeat endoscopy should be performed at 3 to 6 months following optimization of acid suppressive medications. A surveillance interval of 12 months is recommended if an indefinite for dysplasia reading is confirmed on repeat endoscopy in

these individuals. Many patients who are indefinite for dysplasia show regression to nondysplastic BE with subsequent endoscopic evaluation. It is unclear whether some cases of regression are observed due to sampling error.

Nonendoscopic methods for screening are also being studied. Non-endoscopic modalities require minimal intervention, can be done in an office visit and have the potential to be a more ideal choice for mass public screening and surveillance, particularly in patients at low risk for Barrett's esophagus (BE). Various cell collection devices coupled with biomarkers have been used for BE screening. Cytosponge, in combination with TFF3, as well as EsophaCap and EsoCheck have shown promising results when used with various biomarkers.

EsoCheck (Lucid Diagnostics, New York, NY) is a balloon-based sampling device which consists of a collapsible balloon attached to thin silicone catheter connected to a syringe. Once EsoCheck is swallowed and is in the stomach, the balloon is inflated by injecting air into the catheter and withdrawn through the distal 3-6 cm of the esophagus, collecting epithelial cells. After sampling the area described above, the balloon is deflated which leads to its retraction into to the capsule, thereby protecting the sample from bio-contamination from the mid or proximal esophagus as well as oropharynx.

# FDA or Other Governmental Regulatory Approval

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

Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests must meet the general regulatory standards of the Clinical Laboratory Improvement Amendments (CLIA). The WATS3D (CDx Diagnostics), formerly known as EndoCDx, is available under the auspices of the CLIA. Laboratories that offer laboratory-developed tests must be licensed by the CLIA for high-complexity testing. To date, the U.S. Food and Drug Administration has chosen not to require any regulatory review of this test.

The EsoCheck device (Lucid Diagnostics, Inc., New York, NY) has received a 510(k) clearance from the FDA in 2019 while the EsoGuard was granted a breakthrough device designation in February 2020. The EsoGuard test and the EsoCheck device have been proposed as a screening kit for the detection of BE. The specimen is submitted to a laboratory for EsoGuard testing. The

Adjunctive Techniques for Screening and Surveillance of Barrett Esophagus and Esophageal Dysplasia

Policy # 00757
Original Effective Date: 11/08/2021
Current Effective Date: 11/13/2023

EsoGuard uses next generation sequencing bisulfate converted DNA to detect the presence of Vimentin and CyclinA1 methylation signatures at 31 sites within those genes to identify the presence of BE.

# Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The wide-area transepithelial sampling with three-dimensional analysis (WATS3D) is performed during endoscopic examination of the esophagus. The computer-assisted brush biopsy procedure is intended as an adjunct to standard four-quadrant forceps biopsy for screening or surveillance of cancerous or precancerous esophageal lesions and Barrett esophagus (BE).

**Summary of Evidence**

For individuals with a history of Barrett esophagus (BE) who receive standard surveillance with adjunctive WATS3D, the evidence includes a meta-analysis of studies of diagnostic yield, a randomized controlled trial, a physician impact study, a decision analytic model, and a retrospective analysis of the manufacturer database. Relevant outcomes are test validity, overall survival, disease-specific survival, change in disease status, and quality of life. A meta-analysis reported incremental diagnostic yields of 6.9% and 2.4% for any dysplasia or esophageal adenocarcinoma (EAC) or high-grade dysplasia (HGD)/EAC, respectively. These studies are limited by heterogeneity in classification and reporting of test results and selection bias stemming from the enrichment of patients with a prior history of dysplasia. It is also unclear to what extent results obtained from academic centers are generalizable to community-based settings, where adherence to endoscopic biopsy guidelines is poor. In discordant cases where BE or dysplasia were identified only by WATS3D, significant physician management changes included initiation of invasive treatments. Health outcomes stemming from management changes were not reported, and risks associated with over diagnosis and overtreatment require elucidation. Follow-up data on disease progression in these patients are limited. A retrospective analysis of the manufacturer database found a disease

progression rate of 5.79% per patient-year (95% CI, 1.02% to 10.55%) for baseline low-grade dysplasia diagnoses via WATS3D sampling; however, study interpretation is limited as only 16 cases (0.33%) of progression defined as high-grade dysplasia or esophageal adenocarcinoma on follow-up forceps biopsy were identified. A RCT enrolling patients with a recent history of dysplasia reported an absolute increase of 10% in the diagnostic yield of HGD/EAC but did not report on long-term disease progression or mortality outcomes. No direct evidence of clinical utility was identified. Because combined use of WATS3D with standard surveillance is intended to replace the current standard of care for guiding patient management decisions regarding initiation of treatment or surveillance, direct evidence of clinical utility is required. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals at increased risk of BE who undergo standard screening with adjunctive WATS3D, the evidence includes a meta-analysis of studies of diagnostic yield, a physician impact study, a decision analytic model, and a retrospective analysis of the manufacturer database. Relevant outcomes are test validity, overall survival, disease-specific survival, change in disease status, and quality of life. A meta-analysis reported incremental diagnostic yields of 7.2% and 2.1% for any dysplasia/EAC or HGD/EAC, respectively. However, available studies have incomplete descriptions of selection criteria, and it is unclear whether study patients are at increased risk as defined by guideline recommendations for screening. In fact, 2 studies were enriched with women in whom screening is generally not recommended by society guidelines. These studies also noted that detected cases of BE in short-segment patients may actually reflect intestinal metaplasia of the cardia, which is thought to carry a significantly lower risk of cancer development compared to traditional BE. In discordant cases where BE or dysplasia were identified only by WATS3D, significant physician management changes included initiation of invasive treatments. Health outcomes from management changes were not reported, and risks associated with overdiagnosis and overtreatment require elucidation. Follow-up data on disease progression in these patients are limited. A retrospective analysis of the manufacturer database found a disease progression rate of 5.79% per patient-year (95% CI, 1.02% to 10.55%) for baseline low-grade dysplasia diagnoses via WATS3D sampling; however, study interpretation is limited as only 16 cases (0.33%) of progression defined as high-grade dysplasia or esophageal adenocarcinoma on follow-up forceps biopsy were identified. No direct evidence of clinical utility was identified. Because combined use of WATS3D with standard screening is intended to replace the current standard of care for guiding patient management decisions regarding initiation of treatment or surveillance, direct evidence of clinical

utility is required. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals at increased risk of BE who undergo screening with EsoCheck the evidence includes a pilot study. Moinova *et al* performed genome-wide screening to ascertain regions targeted for recurrent aberrant cytosine methylation in BE, identifying high-frequency methylation within the *CCNA1* locus. *CCNA1* DNA methylation was tested as a BE biomarker in cytology brushings of the distal esophagus from 173 individuals with or without BE. *CCNA1* DNA methylation demonstrated an area under the curve (AUC)=0.95 for discriminating BE-related metaplasia and neoplasia cases versus normal, performing identically to methylation of *VIM* DNA, an established BE biomarker. When combined, the resulting two biomarker panel was 95% sensitive and 91% specific. Several limitations were noted. Study was conducted at a single tertiary care institution. Establishing generality will require replication at other centers and in community-based populations. Study population included predominantly male Caucasians, suggesting caution in extrapolating these results to females and other ethnic groups. To avoid difficulties with swallowing the balloon device and the device obtaining adequate sample, authors noted need to focus future enhancements to the device design. Study lacked longitudinal follow-up. Implications of finding positive tests for mVIM and mCCNA1 in endoscopically normal individuals without intestinal metaplasia of stomach or esophagus or in higher risk individuals who are post ablation of dysplastic BE are unknown. Multi-center large-scale clinical trials are currently underway. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome. Use of the EsoGuard test for detection of BE is not considered in accordance with generally accepted standards of medical practice.

# Supplemental Information

**Practice Guidelines and Position Statements**

Guidelines or position statements will be considered for inclusion in ‘Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

***American College of Gastroenterology***

In 2016, the American College of Gastroenterology (ACG) published clinical guidelines on the diagnosis and management of Barrett esophagus (BE) on the basis of a systematic literature review. Guidelines state that "in patients with suspected BE, at least 8 random biopsies should be obtained to maximize the yield of [intestinal metaplasia] on histology. In patients with short (1-2 cm) segments of suspected BE in whom 8 biopsies are unattainable, at least 4 biopsies per cm of circumferential BE, and 1 biopsy per cm in tongues of BE, should be taken (conditional recommendation, low level of evidence)." The guidelines also state that "the role of computer-assisted or wide-field 'brush biopsy' tissue acquisition for increasing the yield of dysplasia is currently under investigation."

In a 2022 guideline update, the ACG stated that they could not make a recommendation on the use of wide-area transepithelial sampling with three-dimensional computer-assisted analysis (WATS3D) and noted that "it is difficult to know how much of the incremental benefit is truly due to more complete sampling of the mucosa by WATS-3D or better detection of dysplasia by the analysis algorithm and how much might be due to overdiagnosis of dysplasia and false-positive examinations by WATS-3D." Limitations of the existing evidence base were summarized, including a lack of studies on adjunctive use for surveillance when forceps biopsies are guided both by white light and chromoendoscopy, a lack of studies reproducing results using pathologists not employed by the manufacturer, and limited stratification of results by grade of dysplasia.

***American Gastroenterological Association***

In 2022, the American Gastroenterological Association issued a clinical practice update addressing new technology and innovation for surveillance and screening in BE. Best practice advice statements were issued based on a review of existing literature and expert opinion. However, statements were not formally rated based on quality of evidence or strength of recommendation. The update states that WATS3D may be used as an adjunctive technique to sample the suspected or established BE segment in addition to the Seattle biopsy protocol.

***American Society of Gastrointestinal Endoscopy***

In 2019, the American Society of Gastrointestinal Endoscopy (ASGE) published guidelines addressing screening and surveillance of BE based on a systematic review and meta-analysis of the literature. Recommendations were drafted at a meeting of the Standards of Practice Committee. The

guidelines state that "in patients with known or suspected BE, we suggest using WATS-3D in addition to [white-light endoscopy] with Seattle protocol biopsy sampling compared with [white-light endoscopy] with Seattle protocol biopsy sampling alone (conditional recommendation, low quality of evidence)." The certainty of the recommendation was downgraded due to risk of bias, inconsistency, and indirectness. Definitions of dysplasia varied across studies, and most studies were manufacturer-funded. The guidelines also note that no recommendation for WATS-3D was made at the initial face-to-face panel meeting. The conditional recommendation was issued following review of additional published literature and a phone conference.

***National Comprehensive Cancer Network***

The National Comprehensive Cancer Network (NCCN) guidelines on esophageal and esophagogastric junction cancers (v.2.2023) state that while WATS3D may help increase the detection of esophageal dysplasia in patients with BE, the utility and accuracy of WATS3D for detecting high-grade dysplasia and adenocarcinoma in patients with BE needs to be evaluated in larger phase III randomized trials.

***Society of American Gastrointestinal and Endoscopic Surgeons***

The Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) Technology and Value Assessment Committee (TVAC) published expert panel recommendations following a safety and efficacy analysis of WATS3D in 2020. Expert panel statements regarding the safety, efficacy, and value of WATS3D included:

- "No significant morbidity or mortality was reported within the literature associated with the WATS3D technology."
- "WATS3D increases diagnostic yield by 38-150% for Barrett's Esophagus, by 40-150% for Low Grade Dysplasia; and by 420% for High Grade Dysplasia; when compared to forceps biopsy alone."
- "WATS3D technique has very high inter-observer agreement for the pathological diagnosis of non-dysplastic and dysplastic Barrett's Esophagus."
- "Increased detection of pre-malignant diseases of the esophagus by the adjunctive use of WATS3D supports screening and surveillance by the adjunctive use of WATS3D during upper endoscopy in appropriate patients."

The committee also noted that "currently, WATS3D is not recommended as a stand-alone substitute for cold forcep biopsies," as the latter still offers the ability to sample specific areas of concern or visible lesions. Additionally, "further research into the use of the WATS3D system as an independent screening or diagnostic modality may be warranted."

**U.S. Preventive Services Task Force Recommendations**
No U.S. Preventive Services Task Force (USPSTF) recommendations for the screening or surveillance of BE and esophageal dysplasia were identified.

**Medicare National Coverage**
There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

**Ongoing and Unpublished Clinical Trials**
Some currently unpublished trials that might influence this review are listed in Table 1.

**Table 1. Summary of Key Trials**

| NCT No. | Trial Name | Planned Enrollment | Completion Date |
|---|---|---|---|
| ***Ongoing*** | | | |
| NCT05056051 | Additive Value of Wide-Area Transepithelial Sampling (WATS3D) in Detection of Recurrence of Intestinal Metaplasia Following Endoscopic Eradication Therapy (EET) for Barrett's Esophagus-Related Neoplasia | 200 | Jun 2024 (recruiting) |
| NCT04312633[a] | CDx Study 906: The Clinical Utility of WATS3D (Wide Area Transepithelial Sampling with Computer-Assisted 3-Dimensional Analysis): A 5-Year Prospective Registry | 90000 | Apr 2025 (recruiting) |

| | | | |
|---|---|---|---|
| NCT05530343 | A Multicenter Randomized Trial of Seattle Biopsy Protocol Versus Wide-Area Transepithelial Sampling in Patients With Barrett's Esophagus Undergoing Surveillance (The SWAT-BE Study) | 2700 | Mar 2026 (recruiting) |
| NCT05642338 | A Multicenter Prospective Cohort Study Comparing Random Biopsies Versus Wide-Area Transepithelial Brush-Sampling (WATS) for Surveillance of Barrett's Esophagus, the WATS-EURO2 Study | 416 | May 2027 (recruiting) |
| ***Unpublished*** | | | |
| NCT02988934[a] | The WATS3D (Wide Area Transepithelial Sample Biopsy with 3-Dimensional Computer-Assisted Analysis) U.S. Registry | 3173/10000 | Feb 2023 (terminated) |

NCT: national clinical trial.
[a] Denotes industry-sponsored or cosponsored trial.

# References

1. Spechler SJ, Sharma P, Souza RF, et al. American Gastroenterological Association medical position statement on the management of Barrett's esophagus. Gastroenterology. Mar 2011; 140(3): 1084-91. PMID 21376940
2. Hirota WK, Loughney TM, Lazas DJ, et al. Specialized intestinal metaplasia, dysplasia, and cancer of the esophagus and esophagogastric junction: prevalence and clinical data. Gastroenterology. Feb 1999; 116(2): 277-85. PMID 9922307
3. Shaheen NJ, Falk GW, Iyer PG, et al. ACG Clinical Guideline: Diagnosis and Management of Barrett's Esophagus. Am J Gastroenterol. Jan 2016; 111(1): 30-50; quiz 51. PMID 26526079
4. Shahsavari D, Kudaravalli P, Yap JEL, Vega KJ. Expanding beyond endoscopy: A review of non-invasive modalities in Barrett's esophagus screening and surveillance. World J Gastroenterol. 2022 Aug 28;28(32):4516-4526. doi: 10.3748/wjg.v28.i32.4516. PMID: 36157931; PMCID: PMC9476875.

5. National Cancer Institute. (2020, June 1). New Technology Gives Patients Access to a 5-Minute, Office-Based Test to Identify Risk for Esophageal Cancer. https://prevention.cancer.gov/news-and-events/blog/NNnew-technology-gives-patients-access-5-minute-office-based-test-identify-risk-esophageal-cancer
6. National Library of Medicine. (2023, January 25). Efficacy of EsoGaurd on Samples Collected Using EsoCheck Versus EGD for the Diagnosis of BE (ESOGUARDBE1). LucidDx sponsored national trial
7. National Library of Medicine. (2023, August 22). Genetic Determinants of Barrett's Esophagus and Esophageal Adenocarcinoma (FBE). Genetic Determinants of Barrett's Esophagus and Esophageal Adenocarcinoma (FBE) by BETRNet
8. Chen WD, Han ZJ, Skoletsky J, et al. Detection in fecal DNA of colon cancer-specific methylation of the nonexpressed vimentin gene. J Natl Cancer Inst 97:1124-1132, 2005. https://academic.oup.com/jnci/article/97/15/1124/2521303
9. Moinova HR, Leidner RS, Ravi L, et al. Aberrant vimentin methylation is characteristic of upper gastrointestinal pathologies. Cancer Epidemiol Biomarkers Prev. 2012 April;21(4): 594-600. Epub 2012/02/09 PNCID: PMC3454489. https://aacrjournals.org/cebp/article/21/4/594/69150/Aberrant-Vimentin-Methylation-Is-Characteristic-of
10. Moinova HR, LaFromboise T, Lutterbaugh JD, et al. Identifying DNA methylation biomarkers for non-endoscopic detection of Barrett's esophagus. Sci Transl Med 2018 Jan 17;10(424). https://www.science.org/doi/10.1126/scitranslmed.aao5848
11. Spechler, Stuart. (September 2023). Barrett's esophagus: Epidemiology, clinical manifestations, and diagnosis. https://www.uptodate.com/contents/barretts-esophagus-epidemiology-clinical-manifestations-and-diagnosis?search=barrett%20esophagus&source=search_result&selectedTitle=1~119&usage_type=default&display_rank=1
12. Spechler SJ, Katzka DA, Fitzgerald RC. New Screening Techniques in Barrett's Esophagus: Great Ideas or Great Practice? Gastroenterology. 2018 May;154(6):1594-1601. doi: 10.1053/j.gastro.2018.03.031. Epub 2018 Mar 23. PMID: 29577931. https://pubmed.ncbi.nlm.nih.gov/29577931/
13. Kadri SR, Lao-Sirieix P, O'Donovan M, Debiram I, Das M, Blazeby JM, Emery J, Boussioutas A, Morris H, Walter FM, Pharoah P, Hardwick RH, Fitzgerald RC. Acceptability and accuracy of a non-endoscopic screening test for Barrett's oesophagus in primary care: cohort study. BMJ.

2010 Sep 10;341:c4372. doi: 10.1136/bmj.c4372. PMID: 20833740; PMCID: PMC2938899. https://pubmed.ncbi.nlm.nih.gov/20833740/

14. Fitzgerald RC, di Pietro M, O'Donovan M, Maroni R, Muldrew B, Debiram-Beecham I, Gehrung M, Offman J, Tripathi M, Smith SG, Aigret B, Walter FM, Rubin G; BEST3 Trial team; Sasieni P. Cytosponge-trefoil factor 3 versus usual care to identify Barrett's oesophagus in a primary care setting: a multicentre, pragmatic, randomised controlled trial. Lancet. 2020 Aug 1;396(10247):333-344. doi: 10.1016/S0140-6736(20)31099-0. PMID: 32738955; PMCID: PMC7408501. https://pubmed.ncbi.nlm.nih.gov/32738955/
15. Lagergren J, Bergstrom R, Lindgren A, et al. Symptomatic gastroesophageal reflux as a risk factor for esophageal adenocarcinoma. N Engl J Med. Mar 18 1999; 340(11): 825-31. PMID 10080844
16. Bennett C, Moayyedi P, Corley DA, et al. BOB CAT: A Large-Scale Review and Delphi Consensus for Management of Barrett's Esophagus With No Dysplasia, Indefinite for, or Low-Grade Dysplasia. Am J Gastroenterol. May 2015; 110(5): 662-82; quiz 683. PMID 25869390
17. Curvers WL, ten Kate FJ, Krishnadath KK, et al. Low-grade dysplasia in Barrett's esophagus: overdiagnosed and underestimated. Am J Gastroenterol. Jul 2010; 105(7): 1523-30. PMID 20461069
18. Fayter D, Corbett M, Heirs M, et al. A systematic review of photodynamic therapy in the treatment of pre-cancerous skin conditions, Barrett's oesophagus and cancers of the biliary tract, brain, head and neck, lung, oesophagus and skin. Health Technol Assess. Jul 2010; 14(37): 1-288. PMID 20663420
19. Sinh P, Anaparthy R, Young PE, et al. Clinical outcomes in patients with a diagnosis of "indefinite for dysplasia" in Barrett's esophagus: a multicenter cohort study. Endoscopy. Aug 2015; 47(8): 669-74. PMID 25910065
20. Yantiss RK. Diagnostic challenges in the pathologic evaluation of Barrett esophagus. Arch Pathol Lab Med. Nov 2010; 134(11): 1589-600. PMID 21043812
21. CDx Diagnostics. WATS3D. 2023; https://www.cdxdiagnostics.com/wats3d.
22. Qumseya B, Sultan S, Bain P, et al. ASGE guideline on screening and surveillance of Barrett's esophagus. Gastrointest Endosc. Sep 2019; 90(3): 335-359.e2. PMID 31439127
23. DeMeester S, Smith C, Severson P, et al. Multicenter randomized controlled trial comparing forceps biopsy sampling with wide-area transepithelial sampling brush for detecting intestinal metaplasia and dysplasia during routine upper endoscopy. Gastrointest Endosc. Jun 2022; 95(6): 1101-1110.e2. PMID 34902373

24. Codipilly DC, Krishna Chandar A, Wang KK, et al. Wide-area transepithelial sampling for dysplasia detection in Barrett's esophagus: a systematic review and meta-analysis. Gastrointest Endosc. Jan 2022; 95(1): 51-59.e7. PMID 34543648
25. Gross SA, Smith MS, Kaul V. Increased detection of Barrett's esophagus and esophageal dysplasia with adjunctive use of wide-area transepithelial sample with three-dimensional computer-assisted analysis (WATS). United European Gastroenterol J. May 2018; 6(4): 529-535. PMID 29881608
26. Smith MS, Ikonomi E, Bhuta R, et al. Wide-area transepithelial sampling with computer-assisted 3-dimensional analysis (WATS) markedly improves detection of esophageal dysplasia and Barrett's esophagus: analysis from a prospective multicenter community-based study. Dis Esophagus. Mar 01 2019; 32(3). PMID 30541019
27. Anandasabapathy S, Sontag S, Graham DY, et al. Computer-assisted brush-biopsy analysis for the detection of dysplasia in a high-risk Barrett's esophagus surveillance population. Dig Dis Sci. Mar 2011; 56(3): 761-6. PMID 20978843
28. Vennalaganti PR, Kaul V, Wang KK, et al. Increased detection of Barrett's esophagus-associated neoplasia using wide-area trans-epithelial sampling: a multicenter, prospective, randomized trial. Gastrointest Endosc. Feb 2018; 87(2): 348-355. PMID 28757316
29. Trindade AJ, Odze RD, Smith MS, et al. Benefit of Adjunctive Wide Area Transepithelial Sampling with 3-Dimensional Computer-Assisted Analysis Plus Forceps Biopsy Based on Barrett's Esophagus Segment Length. Gastrointest Endosc. Apr 04 2023. PMID 37023868
30. Corbett FS, Odze RD, McKinley MJ. Utility of wide-area transepithelial sampling with 3-dimensional computer-assisted analysis as an adjunct to forceps biopsy sampling in the surveillance of patients with Barrett's esophagus after endoscopic eradication therapy. iGIE. December 2022; 1(1): 33-43. DOI: 10.1016/j.igie.2022.10.011.
31. van Munster SN, Leclercq P, Haidry R, et al. Wide-area transepithelial sampling with computer-assisted analysis to detect high grade dysplasia and cancer in Barrett's esophagus: a multicenter randomized study. Endoscopy. Apr 2023; 55(4): 303-310. PMID 36150646
32. Shaheen NJ, Smith MS, Odze RD. Progression of Barrett's esophagus, crypt dysplasia, and low-grade dysplasia diagnosed by wide-area transepithelial sampling with 3-dimensional computer-assisted analysis: a retrospective analysis. Gastrointest Endosc. Mar 2022; 95(3): 410-418.e1. PMID 34537193

33. Singer ME, Smith MS. Wide Area Transepithelial Sampling with Computer-Assisted Analysis (WATS 3D ) Is Cost-Effective in Barrett's Esophagus Screening. Dig Dis Sci. May 2021; 66(5): 1572-1579. PMID 32578042
34. Kaul V, Gross S, Corbett FS, et al. Clinical utility of wide-area transepithelial sampling with three-dimensional computer-assisted analysis (WATS3D) in identifying Barrett's esophagus and associated neoplasia. Dis Esophagus. Dec 07 2020; 33(12). PMID 32607543
35. Shaheen NJ, Falk GW, Iyer PG, et al. Diagnosis and Management of Barrett's Esophagus: An Updated ACG Guideline. Am J Gastroenterol. Apr 01 2022; 117(4): 559-587. PMID 35354777
36. Muthusamy VR, Wani S, Gyawali CP, et al. AGA Clinical Practice Update on New Technology and Innovation for Surveillance and Screening in Barrett's Esophagus: Expert Review. Clin Gastroenterol Hepatol. Dec 2022; 20(12): 2696-2706.e1. PMID 35788412
37. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Esophageal and Esophagogastric Junction Cancers (v.2.2023). March 10, 2023; https://www.nccn.org/professionals/physician_gls/pdf/esophageal.pdf.
38. Docimo S, Al-Mansour M, Tsuda S. SAGES TAVAC safety and efficacy analysis WATS 3D (CDx Diagnostics, Suffern, NY). Surg Endosc. Sep 2020; 34(9): 3743-3747. PMID 32162125

# Policy History

Original Effective Date: 11/08/2021
Current Effective Date: 11/13/2023

| | |
|---|---|
| 10/07/2021 | Medical Policy Committee review |
| 10/13/2021 | Medical Policy Implementation Committee approval. New policy. |
| 12/15/2021 | Coding Update |
| 03/10/2022 | Coding update |
| 10/06/2022 | Medical Policy Committee review |
| 10/11/2022 | Medical Policy Implementation Committee approval. Coverage eligibility unchanged. |
| 10/05/2023 | Medical Policy Committee review |
| 10/11/2023 | Medical Policy Implementation Committee approval. Esophageal brush biopsy tests (e.g., EsoGuard) added to the policy in the investigational statement. Background information added to detail research on other screening |

methods. Information on EsoCheck added to the FDA section. Detail added to Rationale section to support the policy. References updated.



# Coding

*The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2022 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.*

*The responsibility for the content of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines is with Blue Cross and Blue Shield of Louisiana and no endorsement by the AMA is intended or should be implied. The AMA disclaims responsibility for any consequences or liability attributable or related to any use, nonuse or interpretation of information contained in Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. Any use of CPT outside of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines should refer to the most current Current Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.*

CPT is a registered trademark of the American Medical Association.

Adjunctive Techniques for Screening and Surveillance of Barrett Esophagus and Esophageal Dysplasia

Policy # 00757
Original Effective Date: 11/08/2021
Current Effective Date: 11/13/2023

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

| Code Type | Code |
|---|---|
| CPT | 88104, 88305, 88312, 88361<br>Add code effective 11/01/2023: 0114U |
| HCPCS | No codes |
| ICD-10 Diagnosis | All related Diagnoses |

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

‡ Indicated trademarks are the registered trademarks of their respective owners.

**NOTICE:** If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

Adjunctive Techniques for Screening and Surveillance of Barrett Esophagus and Esophageal Dysplasia

Policy # 00757
Original Effective Date: 11/08/2021
Current Effective Date: 11/13/2023

**NOTICE:** Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.