CMS Measure ID/CMS QCDR ID: CAP 18

Measure Title: Mismatch Repair (MMR) or Microsatellite Instability (MSI) Biomarker Testing to Inform Clinical Management and Treatment Decisions in Patients with Primary or Metastatic Colorectal Carcinoma

Measure Specifications

Measure Description	Percentage of all primary or metastatic colorectal carcinoma surgical pathology reports that address the status of biomarker evaluation for mismatch repair (MMR) by immunohistochemistry (biomarkers MLH1, MSH2, MSH6 and PMS2), or microsatellite instability (MSI) by DNA-based testing status, or both. INSTRUCTIONS: This measure is to be reported each time a primary or metastatic colorectal carcinoma pathology report is finalized during the performance period. This measure may be submitted by eligible clinicians who perform the quality actions described in the measure based on the services provided and the measure-specific denominator coding. The results of MMR/MSI testing of a sample are frequently needed at some point during a patient's treatment. Pathologists are uniquely well positioned at the time of signing out the surgical pathology report to detail the disposition of MMR/MSI testing for that sample. Referring physicians depend on both the pathologists' interpretations of and any recommendations for tests in order to provide quality patient care. If the status is not indicated in each pathology report for the patient, important tests may be missed or unnecessary repeat testing may be performed delaying treatment and increasing cost. This measure monitors the success of pathologists in effectively communicating this important information for the purpose of care coordination and efficient use of resources.
Denominator Statement	All surgical pathology reports for primary or metastatic colorectal carcinoma in either biopsy or resection specimen. CPT©: 88305, 88307, 88309 **AND** ICD10: • C18.0: Malignant neoplasm of cecum • C18.2: Malignant neoplasm of ascending colon • C18.3: Malignant neoplasm of hepatic flexure • C18.4: Malignant neoplasm of transverse colon • C18.5: Malignant neoplasm of splenic flexure • C18.6: Malignant neoplasm of descending colon • C18.7: Malignant neoplasm of sigmoid colon • C18.8: Malignant neoplasm of overlapping sites of colon • C18.9: Malignant neoplasm of colon, unspecified • C19: Malignant neoplasm of rectosigmoid junction • C20: Malignant neoplasm of rectum • C78.0: Secondary malignant neoplasm of lung • C78.1: Secondary malignant neoplasm of mediastinum

	• C78.2: Secondary malignant neoplasm of pleura • C78.3: Secondary malignant neoplasm of other and unspecified respiratory organs • C78.4: Secondary malignant neoplasm of small intestine • C78.5: Secondary malignant neoplasm of large intestine and rectum • C78.6: Secondary malignant neoplasm of retroperitoneum and peritoneum • C78.7: Secondary malignant neoplasm of liver and intrahepatic bile duct • C78.8: Secondary malignant neoplasm of other and unspecified digestive organs • C79.0: Secondary malignant neoplasm of kidney and renal pelvis • C79.01: Secondary malignant neoplasm of right kidney and renal pelvis • C79.02: Secondary malignant neoplasm of left kidney and renal pelvis • C79.1: Secondary malignant neoplasm of bladder and other and unspecified urinary organs • C79.10: Secondary malignant neoplasm of unspecified urinary organs • C79.11: Secondary malignant neoplasm of bladder • C79.19: Secondary malignant neoplasm of other urinary organs • C79.2: Secondary malignant neoplasm of skin • C79.3: Secondary malignant neoplasm of brain and cerebral meninges • C79.31: Secondary malignant neoplasm of brain • C79.32: Secondary malignant neoplasm of cerebral meninges • C79.4: Secondary malignant neoplasm of other and unspecified parts of nervous system • C79.40: Secondary malignant neoplasm of unspecified part of nervous system • C79.49: Secondary malignant neoplasm of other parts of nervous system • C79.5: Secondary malignant neoplasm of bone and bone marrow • C79.51: Secondary malignant neoplasm of bone • C79.52: Secondary malignant neoplasm of bone marrow • C79.6: Secondary malignant neoplasm of ovary • C79.60: Secondary malignant neoplasm of unspecified ovary • C79.61: Secondary malignant neoplasm of right ovary • C79.62: Secondary malignant neoplasm of left ovary C79.7: • C79.7: Secondary malignant neoplasm of adrenal gland • C79.70: Secondary malignant neoplasm of unspecified adrenal gland • C79.71: Secondary malignant neoplasm of right adrenal gland • C79.72: Secondary malignant neoplasm of left adrenal gland C79.8: • C79.8: Secondary malignant neoplasm of other specified sites • C79.81: Secondary malignant neoplasm of breast • C79.82: Secondary malignant neoplasm of genital organs

	• C79.89: Secondary malignant neoplasm of other specified sites • C79.9: Secondary malignant neoplasm of unspecified site
Denominator Exclusions	None
Denominator Exceptions	Documentation of reason(s) MMR, MSI, or both tests were not performed (e.g., payor-related limitations, patients receiving hospice)
Numerator Statement	Surgical pathology reports that contain impression or conclusion of, or recommendation for testing of MMR, MSI, or both. Numerator guidance: This measure requires that immunohistochemistry (IHC) for the four MMR proteins (MLH1, MSH2, MSH6 and PMS2); or MSI by DNA-based testing; or both are addressed in the surgical pathology report for biopsy or resection specimens with primary or metastatic colorectal carcinoma present. A short note can be made in the final report, such as or combination of: • No loss of nuclear expression of MMR proteins • Loss of nuclear expression of MMR proteins (intact expression) • Microsatellite instability (MSI) • Microsatellite instability high (MSI-H) • Microsatellite instability low (MSI-L) • Microsatellite stable (MSS) • MMR, MSI, or both previously performed • MMR, MSI, or both recommended • MMR, MSI, or both cannot be determined MMR/MSI status may be derived from either the primary or a reference laboratory.
Numerator Exclusions	None
Measure Information	
NQS Domain	Communication and Care Coordination
Meaningful Measures Area(s)	Transfer of Health Information and Interoperability
Meaningful Measure Rationale	Detection of defective mismatch repair in colorectal carcinomas is important for detection of Lynch syndrome (hereditary nonpolyposis colorectal cancer syndrome [HNPCC]), which accounts for approximately 2% to 4% of all colorectal carcinomas and has clinical implications for treatment of the affected patient and family members (1,2). NCCN recommends that all patients with a personal history of colon or rectal cancer should have MMR or MSI testing (3). In the Molecular Biomarkers for the Evaluation of

Colorectal Cancer guideline from the American Society for Clinical Pathology, College of American Pathologists, Association for Molecular Pathology, and American Society of Clinical Oncology it is recommended that mismatch repair status testing in patients with colorectal cancers is necessary for the identification of patients at high risk for Lynch syndrome and/or prognostic stratification (1).

One of two different initial tests can be performed on colorectal specimens to identify individuals who might have Lynch Syndrome: 1) IHC for MMR protein expression, which is often diminished because of mutation; or 2) analysis for microsatellite instability (MSI), which results from MMR deficiency NCCN guidelines state IHC and MSI on newly diagnosed colorectal and endometrial cancers regardless of family history to determine Lynch Syndrome, is cost effective and has been confirmed for colorectal cancer and endorsed by the Evaluation of Genomic Applications in Practice and Prevention (EGAPP) working group at the CDC, the US Multi-Society Task Force on Colorectal Cancer, and the American Gastroenterological Association (5).

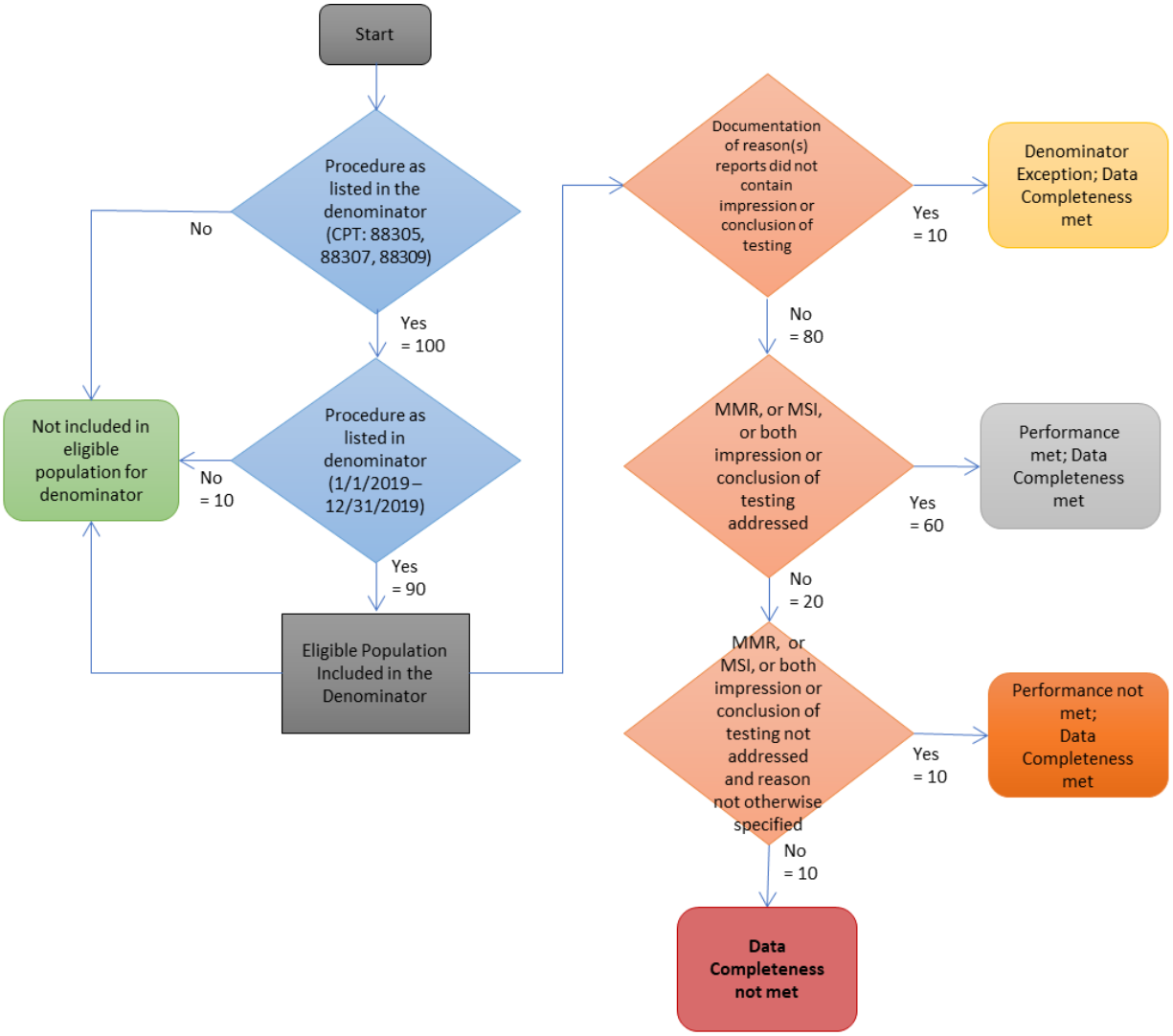
The measure is designed to account for situations where it is not appropriate, safe or possible to obtain MMR or MSI evaluation due to the patient receiving hospice or palliative care, the patient is not at risk for Lynch syndrome (hereditary nonpolyposis colorectal cancer syndrome [HNPCC]), or resources to perform the evaluation are not available. In addition, it is intended to reflect factors relating to patient choice. For all colorectal adenocarcinoma or secondary malignancy from colorectal adenocarcinoma cases, whether MMR, MSI, or both were conducted or not, a standard statement addressing MMR, MSI or both should be included in pathology reports.

1. Rubenstein JH, Enns R, Heidelbaugh J, et al. American Gastroenterological Association Institute guideline on the diagnosis and management of Lynch syndrome. Gastroenterology. 2015;149:777–782.
2. Schmeler KM, Lynch HT, Chen LM, et al. Prophylactic surgery to reduce the risk of gynecologic cancers in the Lynch syndrome. N Engl J Med. 2006;354:261–269.
3. Meyers, M., M. W. Wagner, H. S. Hwang, T. J. Kinsella, and D. A. Boothman. Role of the hMLH1 DNA mismatch repair protein in fluoropyrimidine-mediated cell death and cell cycle responses. Cancer Res 2001. 61:5193–5201.
4. Sepulveda AR, et al. Molecular Biomarkers for the Evaluation of Colorectal Cancer: Guideline from the American Society for Clinical Pathology, College of American Pathologists, Association for Molecular Pathology, and American Society of Clinical Oncology. Arch Pathol Lab Med. 2017 May;141(5):625-657.
5. Benson, AB, et al. National Comprehensive Cancer Network (NCCN) Guidelines Insights. Colon Cancer, Version 2.2018. J Natl Compr Canc Netw 2018;16:359-369.

Measure Type	Process
Data Source	Laboratory Information Systems; pathology reports
Summary of Performance Gap Evidence	In May 2017, the American Society for Clinical Pathology (ASCP), the College of American Pathologists (CAP), the Association for Molecular Pathology (AMP), and the American Society of Clinical Oncology (ASCO) collaborated to develop a clinical practice guideline on molecular biomarker testing for patients with early and advanced colorectal cancer. This evidence-based clinical practice guideline was developed to help establish standard molecular biomarker testing, guide targeted therapy decisions, and advance personalized care for these patients (1). Prior to the release of this guideline, the utility of incorporating prognostic biomarkers in the management of patients with CRC had not been well defined in clinical practice and treatment decisions are not made based on prognostic markers, despite in vitro data suggesting that 5-FU–based therapies do not work in these cancers (2-4). However, as chemotherapeutic regimens become refined and as panels of prognostic markers are put in place to determine which CRC patients should receive therapy, these data will become essential. Laboratories and regulatory agencies are faced with challenges to rapidly and efficiently provide new test results for the management of patients with cancer. There is a need for current evidence-based recommendations for the molecular testing of CRC tissues to guide targeted therapies and conventional chemotherapy regimens. Therefore, the current evidence-based recommendations for the molecular testing of CRC tissues were developed so that new advances in the molecular testing for clinical management of CRC can be integrated (1). 1. Sepulveda AR, et al. Molecular Biomarkers for the Evaluation of Colorectal Cancer: Guideline from the American Society for Clinical Pathology, College of American Pathologists, Association for Molecular Pathology, and American Society of Clinical Oncology. Arch Pathol Lab Med. 2017 May;141(5):625-657. 2. Claij, N. and H. te Riele. Microsatellite instability in human cancer: a prognostic marker for chemotherapy? Exp Cell Res 1999. 246:1–10. 3. Fink, D., S. Aebi , and S. B. Howell . The role of DNA mismatch repair in drug resistance. Clin Cancer Res 1998. 4:1–6. 4. Meyers, M., M. W. Wagner, H. S. Hwang, T. J. Kinsella, and D. A. Boothman. Role of the hMLH1 DNA mismatch repair protein in fluoropyrimidine-mediated cell death and cell cycle responses. Cancer Res 2001. 61:5193–5201.
Measure Owner	College of American Pathologists
NQF ID	N/A

Number of Performance Rates	1
Overall Performance Rate	1st Performance Rate
High-priority	Yes
Improvement Notation	Inverse Measure: No **Proportional Measure: Yes (Higher score indicates better quality)** Continuous Variable Measure: No Ratio Measure: No Risk-adjusted: No
Specialty	Pathology
Current Clinical Guideline the Measure is Derived From	Clinicians should order mismatch repair (MMR) status testing in patients with colorectal cancers for the identification of patients at high risk for Lynch syndrome and/or prognostic stratification (Strong recommendation) (1). Universal MMR* or MSI* testing is recommended in all patients with a personal history of colon or rectal cancer (Strong recommendation) (2). 1. Sepulveda AR, et al. Molecular Biomarkers for the Evaluation of Colorectal Cancer: Guideline from the American Society for Clinical Pathology, College of American Pathologists, Association for Molecular Pathology, and American Society of Clinical Oncology. Arch Pathol Lab Med. 2017 May;141(5):625-657. 2. Benson, AB, et al. National Comprehensive Cancer Network (NCCN) Guidelines Insights. Colon Cancer, Version 2.2018. J Natl Compr Canc Netw 2018;16:359-369.

Measure Flow



Data Completeness =
Denominator Exceptions + Performance Met + Performance Not Met / Eligible Population = 10 + 60 + 10 / 90 = 88%

Performance Rate =
Performance Met / Data completeness Numerator – Denominator Exceptions = 60 / 80 = 75%