REGIONAL MEDICAL LABORATORY

MEMORANDUM

To: All RML Clients
From: Gerald C. Miller, Ph.D., D(ABMLI), Chief of Microbiology and Immunology
Kat Herman, MLS(ASCP)cmSM, Manager of Microbiology
Date: 1/6/2020
Subject: Screening for Colorectal Cancer

Colorectal cancer (CRC) is a common and potentially lethal cancer. Successful screening is very valuable since it can trigger removal of premalignant adenomas and localized cancer, aiding in prevention of CRC and CRC related deaths. Both the incidence and mortality rates from CRC have been declining in the United States, with death rates from CRC declining on average 2.7% each year between 2004 to 2013. One model suggests that screening may account for 53% of the observed reduction in CRC mortality. Most colorectal cancers arise from adenomas, many of which are polyps that progress from small to large polyps, and then to dysplasia and ultimately, cancer. Neoplastic changes result from both inherited and acquired genetic defects. The progression from adenoma to carcinoma, when it occurs, takes at least 10 years on average.

Two important aspects must be considered for CRC screening. First being the guidance to clinicians on age to start and stop CRC screening and frequency of screening. The other aspect addresses optimal screening tests in asymptomatic, average-risk adults. The following **guidance statements do not address surveillance in patients with previously detected adenomatous polyps or diagnosis in persons with signs or symptoms compatible with CRC.**

The main recommendations of the guidance, published in the November 5, 2019 issue of *Annals of Internal Medicine*, were the following:

- All adults ages 50 to 75 of average risk should be screened
- Suggested tests and intervals include: fecal immunochemical testing (FIT) or high-sensitivity guaiac-based fecal occult blood testing (gFOBT) every 2 years, colonoscopy every 10 years, or flexible sigmoidoscopy every 10 years plus FIT every 2 years
- Screening should not be done in average-risk adults older than age 75 or in adults with a life expectancy of less than 10 years

Clinicians should select the CRC screening test in consultation with patients after discussing the benefits, harms, costs, availability, frequency, and patient preferences, advising that all stool tests should be done on voided samples rather than on those obtained from digital rectal examination.

Clinicians should perform individualized assessment of risk for CRC in all adults. Qaseem et.al., authors of the article in the *Annals of Internal Medicine*, noted that risk is elevated in individuals with a family history of CRC, long-standing inflammatory bowel disease, genetic syndromes such as familial adenomatous polyposis, or a personal history of previous CRC or adenomatous polyps.

Other risk factors for CRC include male sex and older age. However the authors stated that "although there is some discussion regarding differences by race and ethnicity, it is not clear if these differences can be attributed to racial differences or health disparities and inequity in screening, follow-ups, and treatments". The current screening guidelines of the U.S. Preventive Services Task Force (USPSTF) advise that all average-risk asymptomatic people be screened from age 50 through age 75 and that select individuals ages 76 to 85 be screened as risk factors and history warrant. Individuals over age 85 should not be screened. USPSTF also recommends annual FIT or FOBT screening and FIT plus a stool DNA panel (sDNA) every 1 to 3 years. Recommendations have varied across such groups as the American Cancer Society (ACS). American College of Radiology, U.S. Multi-Society Task Force on Colorectal Cancer and USPSTF.

Currently recommended screening tests for CRC are either stool-based or those that visualize the colon. Screening tests can improve disease prognosis by detecting early-stage treatable cancers or even adenomas that can progress to cancers. Stool-based tests rely on detection of human hemoglobin and/or DNA, often released into the stool when adenomas or cancer are present. Endoscopic procedures can detect and even prevent cancer, when adenomatous polyps are removed prior to malignant transformation. At the current time, several stool-based screening tests are commercially available and recommended by guideline groups, including the Fecal Immunochemical Test (FIT) and the Cologuard test. Both tests are clinically acceptable options, but have some key differences in their techniques, availability, convenience, comfort and cost (See table 1 below). In considering which stool-based test to select, it is important to review these differences and understand their impact on the patient. **The best test is the one that the patient is willing and able to do**, after an informed shared decision-making process with the clinician. The decision must take into consideration the patient's willingness to collect a stool specimen, particularly if the stool specimen needs to be a large sample as required by Cologuard. For this reason, the Fecal Immunochemical Test (FIT) test collection process is often more acceptable to patients. Furthermore, it is also important to note that the Fecal Immunochemical Test (FIT) is now recommended to be performed every 2 years and the Cologuard every 3 years. A positive result from either test will reflex to a colonoscopy. **RML recommends the use of the Fecal Immunochemical Test (FIT: RML test code 3510285) for routine screening for CRC. An in-depth comparison of both testing options can be found further down in this document.**

Please contact Gerald C. Miller, Ph.D., D(ABMLI) Chief of Microbiology and Immunology, or Kat Herman, MLS(ASCP)cmSM at 918-744-2553 if you have questions.

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Table I. Comparison of the FIT (Fecal Immunochemical Test) and Cologuard

	FIT (OC-Auto)	Cologuard
Manufacturer	Polymedco	Exact Sciences
Pooled Sensitivity*	79% (73-88%)	92.30%
Pooled Specificity	94% (91-96%)	86.60%
False Positive Rate	3.60%	10.20%
Screening Interval	1 year; recent data demonstrates that 2 years would be	3 years; however, optimal time has not been determined
Test Principle	Immunoassay; human stool Hgb	Immunoassay & molecular; human stool Hgb and DNA
Specimen Collection**	Dip the probe into the feces on the floating paper & insert	Place stool in bucket-like container, patient adds buffer;
Number samples required	One	Two: one bucket-like container and one bottle (same
Sample volume required	0.01 gram	≤300 grams; lab will notify patient if volume is insufficient
Specimen Stability	15 days at room temp	Exact Sciences MUST receive the specimen within 72
Results Available	24-48 hours	Results will come from Exact Sciences in 2 weeks

Insurance/Billing:

	FIT (OC-Auto)	Cologuard
Commercial Payers	*Per the Affordable Care Act and as documented on*	*Covered by most private insurers with no co-pay or*
Medicare or Medicaid	*Covered with no co-pay or deductible for eligible patients*	*Covered with no co-pay or deductible for eligible patients*
Self Pay:		
Per Test (self-pay)	Up to $37.48 ***	Up to $649.00
Ten Year Cost (self-pay)	Up to $374.80 ***	Up to $1947.00
RML Test Code/CPT Code	3510285/82274	

** Regarding **effectiveness**, it is often sited that Cologuard has a sensitivity of 92% compared with the FIT's sensitivity of 79%; however, it is important to recognize that FIT is performed yearly and Cologuard every three years. The increased frequency of the FIT test improves the "functional" sensitivity over the entire screening period (50-75 years of age). Also important to consider is that the Cologuard has a 10.2% false positive rate and a colonoscopy is recommended for all positive stool based tests. The FIT test has a 3.6% false positive rate.*

***Regarding **convenience**, the Cologuard is every three years and FIT is yearly. FIT requires only a small fecal aliquot yearly whereby Cologuard requires collection of an entire bowel movement (requiring <300 g in a bucket container and a small aliquot into a bottle).*

****Discounts applied for early payment or financial assistance.*

[1] *Services must be ordered by a provider in the health plan's network.*

[2] *Based on the most common insurance companies 2018 benefit plans.*

Regional Medical Laboratory, Inc. | 4142 S. Mingo Road, Tulsa, OK 74146 | 918-744-2553