Screening for Colorectal Cancer

Eric M. Montminy, MD[a], Albert Jang, MD[b], Michael Conner, MD[b], Jordan J. Karlitz, MD[c,d,*]

KEYWORDS

• Colorectal cancer • Screening • Epidemiology

KEY POINTS

- Colorectal cancer screening is available to providers in primary care settings to improve outcomes in colorectal cancer morbidity and mortality.
- Multiple colorectal cancer screening modalities are available to patients, with colonoscopy remaining the gold standard.
- Colorectal cancer screening rates are not optimized in many parts of the United States, with important barriers to screening including lack of health care provider recommendations and cost.
- It is important to identify higher-risk patients, including those with a family history of colorectal cancer or other cancers, so that earlier screening and possible genetic testing can be performed.

INTRODUCTION

Colorectal cancer (CRC) is the third most common cancer, excluding skin, to be diagnosed in men and women in the United States. The implementation of CRC screening for the detection of premalignant polyps has led to improvements in cancer incidence and survival. Several modalities for screening are available with varying degrees of sensitivity and specificity, but direct visualization with colonoscopy remains the gold standard for screening. This article provides context and guidance for clinicians preparing to discuss initiation of screening with patients.

[a] Division of Gastroenterology, Tulane University School of Medicine, 1430 Tulane Avenue, New Orleans, LA 70112, USA; [b] Department of Internal Medicine, Tulane University School of Medicine, 1430 Tulane Avenue, New Orleans, LA 70112, USA; [c] Southeast Louisiana Veterans Health Care System, Gastroenterology Section, 2400 Canal St, Medicine Service, Ste 3H, New Orleans, LA 70119, USA; [d] Division of Gastroenterology, Tulane University School of Medicine, New Orleans, LA 70112, USA
* Corresponding author.
E-mail address: jkarlitz@tulane.edu

Med Clin N Am 104 (2020) 1023–1036
https://doi.org/10.1016/j.mcna.2020.08.004
0025-7125/20/Published by Elsevier Inc.
medical.theclinics.com

BURDEN OF COLORECTAL CANCER IN UNITED STATES

The CRC mortality in the United States is currently the second highest of all cancers (after lung) for men and women combined. According to the National Cancer Institute, in 2016 the prevalence of CRC was estimated to be 1.3 million cases in the United States.[1] Current 2020 United States predictions estimate approximately 150,000 patients will be diagnosed with CRC, with more than 53,000 deaths.[2] Five-year survival rates range from 90% with localized disease to 14% with metastases, with overall survival rate at any stage of 65%. Lifetime risk of developing CRC is approximately 5%.[2]

Disparities between incidence and survival exist among different ethnic groups in the United States (**Fig. 1**).[2,3] Comparing ethnicities, African Americans consistently have significantly increased mortality and decreased 5-year survival. African Americans have CRC incidence rates of 53.8 per 100,000 for men and 39.9 per 100,000 for women, the highest incidence rates for any ethnic group.[4] White CRC incidence rates of 44.0 per 100,000 for men and 33.9 per 100,000 for women have been observed.[2] Hispanic Americans currently show lower incidences compared with white people: 40.8 per 100,000 for men and 28.7 per 100,000 for women.[2] Asian Americans continue to show the lowest incidence among all ethnic groups: 35.3 per 100,000 for men and 25.7 per 100,000 for women.[2] American Indian and Alaska Natives have a very high burden of disease, showing an incidence of 48.5 per 100,000 for men and 39.1 per 100,000 for women.[2]

Hispanic people are the fastest-growing minority population in the United States, and their population is younger than the average American population, so incidence rates are expected to increase in the upcoming decades.[5,6] Moreover, Hispanic people show higher mortalities from metastatic CRC compared with white people, and in turn, Hispanic people may show a higher mortality burden from CRC in the coming decades.[5,6]

Despite a lower incidence of CRC relative to other ethnicities, CRC is still the most common cancer diagnosed among Asian Americans.[7] Among east and southeast Asians, CRC screening rates are lower compared with African Americans and white people but higher compared with Hispanic people.[7] Importantly, wide variations in screening exist among individual Asian subgroups.[7]

The American Indian and Alaskan Native population also has CRC incidence and mortality that are higher than those of white people. Although incidence and mortality declined among white people in recent decades, it did not change for the American Indian and Alaskan Native population.[8] American Indian and Alaskan Native

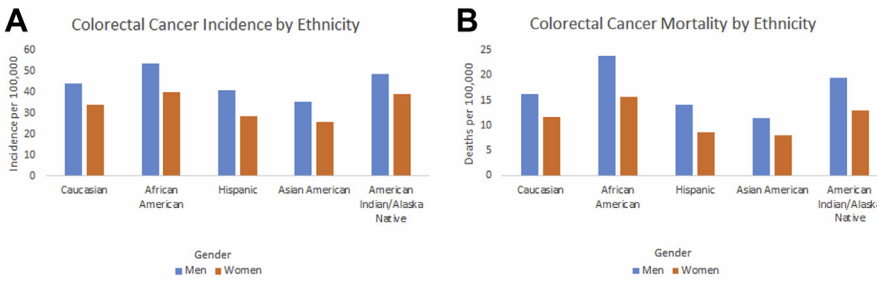

Fig. 1. CRC incidence (*A*) and mortality (*B*) rates in men and women by ethnicity, 2012 to 2017. African American men and women have the highest incidence and mortalities compared with other ethnicities. (*Adapted from* Siegel RL, Miller KD, Sauer AG, et al. Colorectal Cancer Statistics, 2020. CA Cancer J Clin. 2020; 70: 7-30. With permission.)

populations also have lower CRC screening rates compared with African Americans and white people.[9]

Regarding age, approximately 50% of all cases are diagnosed by age 65 years, and nearly 80% are diagnosed by age 80 years.[2] Recent attention has been directed toward so-called early-onset CRC.[2] Observations using Surveillance, Epidemiology, and End Results (SEER) analysis have shown acceleration of early-onset CRC incidence in patients aged 20 to 49 years over the last 3 decades.[2] Reasons for increasing early-onset CRC incidence are unclear at this time but may include alcohol consumption, diets consisting of red and processed meat, tobacco abuse, increasing obesity, and advanced endoscopic detection techniques.[10] It is thought that there is a potential underlying birth cohort effect associated with these increasing CRC rates, and increasing incidence has also been seen in 50 to 54-year-olds.[2] A recent study analyzing SEER data in 1-year age increments, as opposed to age range blocks, revealed a steep 46.1% incidence rate increase in CRCs from age 49 to 50 years, and 92.9% of these were invasive (beyond in situ stage).[11] These findings are consistent with a large undetected preclinical cancer burden ultimately diagnosed with screening at age 50 years, which is not reflected in observed SEER incidence rates.

NATURAL HISTORY OF COLORECTAL CANCER DEVELOPMENT

CRC is the umbrella term used for malignant neoplasms associated with various histologies throughout the colon and rectum. Among the various malignant neoplasms, almost all CRC is adenocarcinoma.[8] Adenocarcinomas develop from adenomas, which have varying degrees of dysplasia (potential to develop into an invasive malignancy).[12]

The progression of normal colorectal mucosa to adenoma to adenocarcinoma has been well defined. Several genetic mutations have been identified to initiate and promote the sequence of advancing dysplasia (**Fig. 2**). Most adenomatous polyps begin to develop from previously normal colorectal mucosa after expression of either an inherited or acquired mutation in the adenomatous polyposis coli gene (APC) and/or DNA mismatch repair gene (MMR). Early adenomas then typically progress to higher-risk adenomas if mutations such as K-Ras gene (KRAS) are expressed.

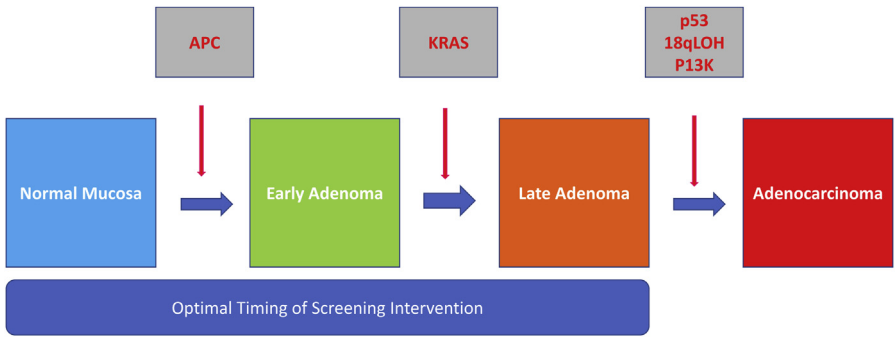

Fig. 2. Typical development of adenocarcinoma from adenoma. Note timing of each mutation along the progression of normal mucosa to adenocarcinoma. Ideally, CRC screening should be performed before the development of adenocarcinoma, when early and late adenomas can be detected and removed. APC, adenomatous polyposis coli; KRAS, K-Ras; PI3K, phosphatidylinositol 3 kinase.

Thereafter, loss of other apoptotic and cellular proliferation regulatory genes may accrue, leading to invasive adenocarcinomas.[12]

Adenomas have varying histologic classifications that hold different malignant potentials. Typical classifications of adenomas include a spectrum of tubular, tubulovillous, and villous histology depending on what percentage of each is visualized on pathology.[13] Tubular adenomas typically possess lower malignant potential, whereas villous adenomas hold higher malignant potential.[13] In general, polyps larger than 1 cm are associated with higher risk for malignancy compared with polyps less than 1 cm.[13] Importantly, all adenomas possess a degree of dysplasia and, in turn, a risk of malignant transformation over time.[13] If possible, adenomas should be removed when identified to minimize the chance of malignant transformation.

In addition, polyps can be defined by a sawtooth architecture visualized histologically with serration.[14] These polyps are often described endoscopically as flat (sessile) polyps and are often found within the right colon (ascending colon and cecum).[14] Depending on size, location, and exact histology, such polyps may be associated with various degrees of malignant potential. Specific guidelines are available focusing on the management and colonoscopy surveillance intervals for such lesions.[15]

COLORECTAL CANCER RISK FACTORS

Both modifiable and nonmodifiable risk factors for CRC have been established, and mitigating these risk factors plays an integral role in CRC prevention (**Table 1**). Modifiable risk factors such as tobacco and alcohol abuse, obesity, processed and red meats, and physical inactivity are abundant in the United States.[16] At the time of initiating CRC screening, modifiable risk factors should be discussed in order to further reduce CRC risk. Nonmodifiable CRC risks include aging, inflammatory bowel disease (ulcerative colitis or Crohn disease), prior abdominal radiation exposure, and family history of CRC or high-risk polyps.[16]

COLORECTAL CANCER RISK FACTORS: FAMILY HISTORY AND GENETIC SYNDROMES

Of the nonmodifiable risk factors for CRC, family history of CRC is significantly impactful. People with a first-degree relative (parent, sibling, or child) who have CRC have a 2 to 4 times risk of developing CRC themselves.[17] A family history of advanced colorectal polyps is also a significant, and underrecognized, CRC risk factor. This history

Table 1
Modifiable and nonmodifiable risk factors associated with the development of colorectal cancer

Risk Factors	
Modifiable	**Nonmodifiable**
Obesity	Aging
Physical inactivity	Inflammatory bowel disease
Tobacco abuse	Abdominal and pelvic radiation
Alcohol abuse	Hereditary CRC Syndromes
Diets high in red and processed meats	Family history of CRC or high-risk polyps
Cooking meats to high temperatures	Personal history of colorectal polyps
	Ethnicity
	Type 2 diabetes mellitus

includes any family history of a tubular adenoma greater than or equal to 1 cm and/or with villous features or high-grade dysplasia regardless of size. In addition, any family history of sessile serrated polyps greater than or equal to 1 cm or cytologic dysplasia and family history of traditional serrated adenomas should be discussed. First-degree relatives of patients with these advanced adenomas have significantly increased risk for CRC (1.68–3.80-fold increase) and advanced adenoma (6.05-fold increase).[18] It is important that providers ask patients not just about a family history of cancer but also about their family history of polyps so that proper risk stratification takes place. It is also recommended that, if an advanced polyp is diagnosed on colonoscopy, the provider who performed the colonoscopy should counsel the patient with the polyp that the patient's first-degree relatives are at increased risk and will need earlier screening (screening guidelines are discussed later).

People with a history of a mendelian cancer syndromes (such as Lynch syndrome) or polyposis syndromes (such as familial adenomatous polyposis or mutY homolog (MUTYH)-associated polyposis) have among the highest risk for CRC.[19] Mendelian CRC syndromes account for about 5% of CRC, with much higher percentages in patients with early-onset CRC.[20] Individuals that are carriers of the underlying genetic mutations can develop cancer at a much younger age than other high-risk groups and must initiate screening as early as their first decade of life depending on the syndrome and underlying mutation. The National Comprehensive Cancer Network (NCCN) "Genetic/Familial High-Risk Assessment: Colorectal" guidelines are an excellent resource that provide continually updated information on syndromic CRC, including information on genetic testing, diagnosis, and surveillance recommendations.[21] The guidelines also provide information on extracolonic cancers that have shown new associations with syndromes, such as breast and prostate cancer in Lynch syndrome.

A thorough family history should always be performed in order to identify patients that may require genetic testing. Knowledge of family history is also critical in order to determine timing of CRC screening in family members (how guidelines differ is discussed later) even if thresholds for need for germline testing are not met. A recent publication revealed that, in patients 40 to 49 years old with CRC, 1 in 4 met criteria for earlier screening based on family history and could have had their cancers detected earlier or prevented altogether if earlier screening had been initiated as per guidelines.[22]

Many of the tools focused on identifying Lynch syndrome are heavily weighted toward obtaining an accurate family history, such as the Prediction Model for MLH1, MSH2, MSH6, PMS2, and EPCAM Gene Mutations (PREMM5 Model).[20,a] This model is a particularly useful online tool in which basic information on personal and family history of cancer is entered into a Web site and a percentage chance of having an underlying Lynch syndrome mutation is quickly provided. A family history of extracolonic cancers may also indicate an underlying syndrome, and hence it is important for providers to ask patients about the patient's family history of all cancer types. For example, uterine cancer is the most common extracolonic cancer in Lynch syndrome, with up to 57% of patients developing uterine cancer depending on the underlying mutation.[21]

[a] The Bethesda guidelines, Amsterdam criteria, and PREMM5 are prediction models used to quantify an individual's risk for carrying a Lynch syndrome–associated mismatch repair gene and then decide whether further genetic testing is indicated.

Patients confirmed to be carriers of any of the mendelian CRC genes should be referred to a specialist in order to initiate screening at the appropriate age and determine intervals for follow-up examinations. Note that hereditary cancer syndromes are frequently under-recognized but carry substantial risk for both patients and family members. It is estimated that 1 in 279 people in the general population are Lynch syndrome carriers but many are unaware that they are carriers.[23] Even in young patients who have been diagnosed with CRC, diagnostic testing for Lynch syndrome is infrequently performed, placing patients and family members at high risk.[24]

It should also be noted that the NCCN guidelines currently recommend that all patients diagnosed with CRC, regardless of age, should undergo tumor testing with microsatellite instability or immunohistochemistry analysis as an initial screen for Lynch syndrome. For polyposis syndromes, it is important for providers to be mindful of the lifetime cumulative number of polyps (not just on a single colonoscopy), which may be overlooked, so that determination of the need for genetic testing can be made.

COLORECTAL CANCER SCREENING EFFECTIVENESS

Colonoscopy

Colonoscopy involves the use of a fiberoptic endoscope to examine the entire length of the colon in a sedated patient after bowel preparation. Of all screening modalities, colonoscopy has been shown to be the gold standard for detection and removal of premalignant colorectal polyps and detection of CRC.[25] Colonoscopy has been validated as an effective and superior CRC screening modality since the 1990s in both average-risk and high-risk patients. Extensive evidence from large randomized controlled trials such as the National Polyp Study Workgroup in 1993 studying colonoscopy with polypectomy in average-risk adults showed decreased incidence of CRC as high as 90% depending on location of cancer.[26] Advantages of colonoscopy include the highest sensitivity and specificity for detecting CRC and premalignant polyps compared with other screening modalities, as well as a potential 10-year screening interval in average-risk patients.[25] Disadvantages of colonoscopy include the need for bowel preparation and sedation as well as possible additional cost sharing not covered by commercial insurance or Medicare/Medicaid.[25] Although rare, colonoscopy carries procedural risks of mucosal injury such as laceration, bleeding, and perforation, as well as infection with instrumentation.

Quality measures for colonoscopy have been introduced to gives providers and patients perspective on screening performance. Metrics such as adenoma detection rate, adequacy of bowel preparation, and cecal withdrawal times have been introduced in order to improve the quality of colonoscopy and patient outcomes.[25] These individual metrics can be discussed with the provider who will be performing the procedure before screening to ensure a high-quality examination.

Stool-Based Screening

Fecal immunochemical testing (FIT) and guaiac fecal occult blood testing (gFOBT) are two stool-based CRC screening tests that are intended for outpatient CRC screening on an annual interval.[25] Both stool-based tests rely on detection of occult volumes of blood components taken up by stool as it passes over a friable cancer. FIT has shown higher CRC detection rates compared with gFOBT, and therefore FIT is primarily used.[27] Of marketed gFOBT kits, the American Cancer Society (ACS) only recommends using the newer, highly sensitivity guaiac test for CRC screening.[28]

FIT shows CRC screening sensitivity rates of approximately 80%, but detection of advanced adenomas is less than that of colonoscopy and has minimal sensitivity for

sessile serrated polyps. At present, the United States Multi-Society Task Force[b] (USMSTF) labels FIT as an alternative tier 1 screening modality for patients opting not to undergo colonoscopy and willing to undergo yearly screening intervals.[25,c] Advantages of CRC screening with FIT center on decreased invasiveness and substantially less cost.[25] These advantages may be a factor for patients who are hesitant to undergo sedation or bowel preparation. Disadvantages include the need for yearly testing, higher false-positive rates compared with colonoscopy, and inability to intervene directly on precancerous lesions at time of screening.[25] Quality initiatives of FIT have primarily focused on improving access to FIT in the primary care setting and ensuring patients with positive FIT are promptly referred for colonoscopy.[25]

The more recently developed FIT-fecal DNA testing has been introduced as another alternative modality for CRC screening. FIT-fecal DNA testing incorporates detection of blood products and abnormal DNA genetic components such as KRAS mutations within stool into 1 test.[29] FIT-DNA testing is performed every 3 years as opposed to annually with traditional FIT. Advantages include increased sensitivity for cancers, advanced adenomas, and serrated polyps compared with FIT alone, although sensitivity is lower than that of colonoscopy.[30] According to the USMSTF, disadvantages primarily involve lower specificity rates (87% for FIT-DNA, 94% for FIT alone) compared with colonoscopy and FIT as well as higher cost.[25,31]

Computed Tomography Colonography (Virtual Colonoscopy)

Computed tomography (CT) colon imaging with air insufflation (known as CT colonography) has been used for CRC screening. CT colonography has been reported to detect CRC with sensitivities as high as 96%, although studies have largely been performed in symptomatic adults.[32] Prior comparisons of CT colonography with colonoscopy have shown CT colonography identifying precancerous adenomas at lower rates compared with colonoscopy.[33,34] CT colonography is associated with radiation exposure and the need for specific radiology facilities. It has been labeled a tier 2 CRC screening option by the USMSTF and may appeal to a niche of patients who are concerned about the risk of colonoscopy.[25] Like colonoscopy, CT colonography requires bowel preparation before an examination in order to optimize cancer detection. In addition, if a polyp is detected, colonoscopy is often recommended for direct visualization and removal.

Video Capsule Endoscopy

Video capsule endoscopy (VCE) involves swallowing a pill-shaped camera device that captures pictures of the intestinal mucosa throughout transit from mouth to anus after bowel preparation. With adequate bowel preparation, VCE has reached a sensitivity of 88% for adenomas larger than 6 mm but performed significantly worse for detection of serrated polyps.[25,35] VCE is not approved by the US Food and Drug Administration for average-risk CRC screening but may be used as an adjunct tool to visualize proximal colon lesions in patients with incomplete screening colonoscopy or patients who are not candidates for colonoscopy.[25]

---

[b] The USMSTF of CRC represents the American College of Gastroenterology (ACG), American Society of Gastrointestinal Endoscopy (ACGE), and American Gastroenterological Association (AGA).

[c] Currently the United States Preventive Services Task Force (USPSTF) does not tier screening modalities and instead highlights that there is convincing evidence that CRC screening substantially reduces deaths in patients 50 to 75 years old.[35]

Flexible Sigmoidoscopy

Flexible sigmoidoscopy is an endoscopic examination of the distal colon typically reaching as far as the splenic flexure. In the past, flexible sigmoidoscopy has been used as an effective CRC screening option for distal CRC; however, this modality has been largely replaced by colonoscopy because of the decreased ability of flexible sigmoidoscopy to detect proximal colon cancer.[25] Like colonoscopy, flexible sigmoidoscopy allows intervention on precancerous polyps at the time of screening and can be performed without sedation, if necessary.[25]

Septin 9 Assay

The Septin 9 assay is a serum-based CRC screening test that is intended to detect levels of Septin 9, a biomarker shed into the bloodstream after CRC development. Although approved for CRC screening, the Septin 9 assay shows markedly inferior sensitivity for the detection of CRC compared with other screening modalities. More recent pooled analyses observed sensitivities as high as 69% and specificity of 92% for CRC detection, but minimal to no adenoma sensitivity.[36]

HOW GUIDELINES DIFFER BETWEEN NATIONAL SOCIETIES' SCREENING RECOMMENDATIONS

American Cancer Society and United States Preventive Services Task Force

The ACS updated guidelines in 2018 to recommend initiating CRC screening in average-risk patients at 45 years old instead of 50 years old. Initiating earlier average-risk screening has been recommended based on increasing early-onset CRC incidence rates and modeling studies focused on life-years gained by initiating screening at 45 versus 50 years old.[37] ACS recommends screening should continue until 75 years old if the patient is in good health with a life expectancy more than 10 years.[37] The decision to continue past 75 years old and up until 85 years old should be based on patient preference, lack of previous screening history, and overall health.[25,37] The ACS recommends offering different screening options, including stool-based tests and structural examinations (such as colonoscopy) and performing the test that is most likely able to be completed.[28] Any abnormal screening test that is not an initial screening colonoscopy must be followed up with a diagnostic colonoscopy. The ACS screening approach is similar to the recommendation from the USPSTF, which recommends choosing a screening option based on patient preference and adherence, as well as medical contraindications and resources/availability.[38]

The United States Multi-Society Task Force on Colorectal Cancer

The USMSTF recommends initiating screening at 50 years old in average-risk individuals, with the exception of average-risk African Americans who should initiate screening at 45 years old. Based on the new ACS screening guidelines in 2018 recommending screening initiation at 45 years old, the USMSTF released a statement reporting that this change may improve early detection and prevention of CRC in younger individuals. The statement also reported that this change only addresses part of the increasing risk of CRC in younger individuals and that prompt assessment of symptoms consistent with CRC remains critical in persons less than 50 years of age.[39] The USMSTF shares similar guidelines to the ACS on screening discontinuation at 75 versus 85 years old.

In contrast with the USPSTF and ACS, the USMSTF recommends a sequential approach, in which health care providers offer patients preferred testing first and, if

Table 2
United States Multi-Society Task Force tier recommendation of screening modalities with respective screening intervals

Tier Recommendation	Screening Modality	Screening Interval
Tier 1	Colonoscopy	Every 10 y
	FIT	Annual
Tier 2	FIT-DNA	Every 3 y
	CT colonography	Every 5 y
	Flexible sigmoidoscopy	Every 5 y
Tier 3	VCE	Every 5 y

declined, offer the next highest-performance testing.[25] Stool-based testing and direct visualization are divided into tiers in order to follow the sequential approach (**Table 2**). Although the USMSTF still reports that the best test is the one that gets done, a tiered approach is recommended in order to have screening options with higher sensitivity and cost-effectiveness completed more frequently.[25] By following this approach and starting with tier 1, colonoscopy should be offered first, but, if refused, FIT is an appropriate second option. If both of these options are refused, the tiered system allows providers to offer the next highest-performing test by moving to tier 2 and then tier 3.

High-Risk Individuals

Most high-risk individuals should start CRC screening at an earlier age, ideally with colonoscopy.[37] Individuals with a family history of CRC or advanced adenomas, but no history of mendelian CRC syndromes (discussed earlier in relation to family history and genetic syndromes), should follow screening recommendations depending on the number of first-degree relatives and their respective ages of diagnosis. Per USMSTF guidelines, individuals with a single first-degree relative diagnosed with CRC or an advanced adenoma before age 60 years or 2 first-degree relatives diagnosed at any age should be screened with colonoscopy starting at age 40 years or 10 years earlier than the relative's diagnosis, whichever is earlier. Examinations can be repeated at 5-year intervals or possibly more frequently depending on findings. Individuals with a single first-degree relative diagnosed with CRC or an advanced adenoma at or after age 60 years can be offered average-risk screening options but beginning at age 40 years.[25]

COLORECTAL CANCER SCREENING IN THE UNITED STATES: HOW CAN IT BE IMPROVED?

Despite local and national initiatives, CRC screening rates among different communities generally are not optimal. At present, screening rates vary in patients aged 50 to 75 years depending on whether they seek screening through private insurance (72% screened), Medicare (62% screened), or a federally funded community clinic (44.1% screened).[40] The National Colorectal Cancer Roundtable (NCCRT) launched the 80% by 2018 initiative, and subsequently the 80% in Every Community initiative, which focus on improving national and individual community CRC screening rates to 80% of their respective populations. The NCCRT continually updates the progress of these initiatives in order to identify disparities in which resources can be focused, including low-income and rural populations and racial/ethnic minority communities,

which can vary both between and within states. The lowest CRC screening rates have been observed in Latin-American, Native American, and Asian-American minority communities.[17] States such as Wyoming, Texas, and Nevada currently show some of the lowest percentages of state-wide populations undergoing CRC screening.[17] In response, the NCCRT has worked with national/local governments, academic institutions, cancer survivor groups, and insurance payers to identify and address screening barriers (**Box 1**). Barriers identified include financial cost of screening, lack of patients established with a primary care physician, so-called therapeutic inertia (ie, resistance to a clinical treatment by a patient or clinician), access to screening, and lack of screening navigators.[41] One of the most important barriers is lack of addressing CRC screening in the primary care setting. With further outreach, NCCRT hopes to reach 80% CRC screening rates in all communities. Clinicians and health care networks can find further tools and resources for improving CRC screening rates in each community through the NCCRT Internet-based platform: www.nccrt.org/resource-center.

KEY RECOMMENDATIONS FOR IMPLEMENTING SCREENING IN THE PRIMARY CARE SETTING

Establishing Patient Expectations

Patients approaching the timing of CRC screening should be adequately informed on expectations of screening goals and options. This discussion ideally should begin in the years leading up to the initiation of screening, because often there are delays between the time discussing CRC screening and the examination occurring. Asking questions such as, "What is your understanding of colorectal screening?" can elicit patient perspective to build on. Thorough discussions of family history of CRC or high-risk polyps can be discussed in the years leading up to screening initiation to determine the appropriate age to begin screening. Family history of CRC (and other types of cancer that may be associated with hereditary syndromes) and high-risk polyps is important to update with each health care maintenance visit because changes in family history can change the timing and interval of screening recommendations for the patient.

In addition, providers should discuss the importance of continued CRC screening during health care maintenance encounters in order to improve patient adherence to screening intervals. Providing easily accessible Web-based and print information on CRC screening to patients in an outpatient office can aid with directing patient attention toward different screening options and recommended screening intervals. Overall goals of screening expectations should be to provide patients with adequate

Box 1
Identified barriers to colorectal cancer screening

Lack of access to a primary care physician
Lack of provider recommendations for screening
Financial cost
Therapeutic Inertia
Lack of access to screening modalities
No access to screening navigators

resources to make informed decisions on screening in order to allow individualization of care.

Screening Availability and Access to Colonoscopy

Providers should understand which screening tests and referral centers are most accessible to patients before initiating CRC screening discussions. With the advent of outpatient endoscopy centers, access to screening colonoscopy and diagnostic colonoscopy if another screening test (eg, stool-based test, CT colonography) is positive has improved, but in some settings access to colonoscopy is still restricted. Patient navigator networks have been incorporated successfully in primary care settings and can be used to optimize access to screening modalities such as colonoscopy and referrals for expedited colonoscopy if another screening test is positive.[42]

Costs of Colorectal Cancer Screening

Commercial and government-provided insurance plans cover most CRC screening modalities. Patients should be provided an understanding of screening cost and potential for cost sharing. For example, health insurance plans established through the Patient Protection and Affordable Care Act removed cost sharing from polypectomy during screening colonoscopy. However, Medicare and Medicaid plans may require patients undergoing screening colonoscopy to participate with cost sharing if polypectomy is performed during the examination.[43] Ongoing federal legislation is being reviewed in order to address these cost-sharing measures.[44,45] It is beneficial for patients to have a discussion with insurance providers to understand payment issues associated with screening options.

DISCLOSURE

J.J. Karlitz serves as consultant to Exact Sciences Corporation as well as being a consultant and part of the speakers bureau for Myriad Genetics. Dr J.J. Karlitz has an equity position in Gastro Girl.

DISCLAIMER

The contents in this article do not necessarily reflect the views of the Department of Veterans Affairs or the US government.

REFERENCES

1. Surveillance, Epidemiology, and End results (SEER) Program. SEER*Stat Database: mortality-all COD, Aggregated with state, Total US (1969-2017) <Katrina/Rita population Adjustment>. National cancer Institute, Division of cancer Control and population Sciences, surveillance Research Program, cancer Statistics Branch; 2019; underlying mortality data provided. National Center for Health Statistics; 2019.
2. Siegel RL, Miller KD, Sauer AG, et al. Colorectal Cancer Statistics, 2020. CA Cancer J Clin 2020;70:7–30.
3. Montminy EM, Karlitz JJ, Landreneau SW. Progress of colorectal cancer screening in United States: past achievements and future challenges. Prev Med 2019;120:78–84.
4. DeSantis CE, Miller KD, Sauer AG, et al. Cancer Statistics for African Americans, 2019. CA Cancer J Clin 2019;69:211–33.

5. Hernandez-Nieto R, Gutierrez MC, Moreno-Fernandez F. Hispanic map of the United States 2017 2017. Available at: http://cervantesobservatorio.fas.harvard.edu/sites/default/files/hispanic_map_2017en.pdf. Accessed April 3, 2020.
6. Barzi A, Yang D, Mostofizadh S, et al. Trends in colorectal cancer mortality in hispanics: a SEER analysis. Oncotarget 2012;8:108771–7.
7. Hwang H. Colorectal cancer screening among Asian Americans. Asian Pac J Cancer Prev 2013;14:4025–32.
8. Fleming M, Ravula S, Tatishchev S, et al. Colorectal carcinoma: pathologic aspects. J Gastrointest Oncol 2012;3:153–73.
9. Johnson-Jennings MD, Tarraf W, Hill KX, et al. United States colorectal cancer screening practices among american indians/alaska natives, blacks, and non-hispanic whites in the New Millennium (2001 to 2010). Cancer 2014;120:3192–299.
10. Mauri G, Sartore-Bianchi A, Russo AG, et al. Early-onset colorectal cancer in young individuals. Mol Oncol 2019;13:109–31.
11. Abualkhair WH, Zhou M, Ahnen D, et al. Trends in incidence of early-onset colorectal cancer in the United States among those approaching screening age. JAMA Netw Open 2020;3:e1920407.
12. Carvalho B, Sillars-Hardebol AH, Postma C. Colorectal adenoma to carcinoma progression is accompanied by changes in gene expression associated with aging, chromosomal instability, and fatty acid metabolism. Cell Oncol (Dordr) 2012;35:53–63.
13. Calderwood AH, Lasser KE, Roy HK. Colon adenoma features and their impact on risk of future advanced adenomas and colorectal cancer. World J Gastrointest Oncol 2016;8:826–34.
14. Rex DK, Ahnen DJ, Baron JA, et al. Serrated lesions of the colorectum: review and recommendations from an expert panel. Am J Gastroenterol 2012;107:1315–30.
15. Lieberman DA, Rex DK, Winawer SJ, et al. Guidelines for colonoscopy surveillance after screening and polypectomy: a consensus update by the US multisociety task force on colorectal cancer. Gastroenterology 2012;143:844–57.
16. Johnson CM, Wei C, Ensor JE, et al. Meta-analyses of colorectal cancer risk factors. Cancer Causes Control 2013;24:1207–22.
17. American Cancer Society. Colorectal cancer facts & figures 2020-2022. Atlanta (GA): American Cancer Society; 2020.
18. Molmenti CL, Kolb JM, Karlitz JJ. Advanced colorectal polyps on colonoscopy: a trigger for earlier screening of family members. Am J Gastroenterol 2020;115:311–4.
19. Syngal S, Brand RE, Church JM. ACG clinical guideline: genetic testing and management of hereditary gastrointestinal cancer syndromes. Am J Gastroenterol 2015;110:223–63.
20. Tomlinson Ian. The mendelian colorectal cancer syndromes. Ann Clin Biochem 2015;52:690–2.
21. National Comprehensive Cancer Network. Genetic/Familial High-Risk Assessment: Colorectal. Available at: https://www.nccn.org/professionals/physician_gls/default.aspx#genetics_colon. Accessed June 14, 2020.
22. Gupta S, Bharti B, Ahnen DJ, et al. Potential impact of family history–based screening guidelines on the detection of early-onset colorectal cancer. Cancer 2020;126:3013–20.
23. Yurgelun MB, Hampel H. Recent advances in lynch syndrome: diagnosis, treatment, and cancer prevention. Am Soc Clin Oncol Educ Book 2018;38:101–9.

24. Karlitz JJ, Hsieh MC, Liu Y, et al. Population-based lynch syndrome screening by microsatellite instability in patients ≤50: prevalence, testing determinants, and result availability prior to colon surgery. Am J Gastroenterol 2015;110:944–58.
25. Rex DK, Boland R, Dominitz JA, et al. Colorectal cancer screening: recommendations for physicians and patients from the U.S. multi-society task force on colorectal cancer. Am J Gastroenterol 2017;112:1016–30.
26. Winawer SJ, Zauber AG, Ho MN, et al. Prevention of colorectal cancer by colonoscopic polypectomy. the national polyp study workgroup. N Engl J Med 1993; 329:1977–81.
27. Kupper BE, Junior SA, Nakagawa WT, et al. Comparison between an Immunochemical Fecal Occult Blood Test and a Guaiac Based Fecal Occult Blood Test in Detection of Adenomas and Colorectal Cancer. Appl Cancer Res 2018;38(5).
28. American Cancer Society. Colorectal cancer screening tests. 2018. Available at: https://www.cancer.org/cancer/colon-rectal-cancer/detection-diagnosis-staging/screening-tests-used.html. Accessed July 24,2020.
29. Imperiale TF, Ransohoff DF, Itzkowitz SH, et al. Multitarget stool DNA testing for colorectal-cancer screening. N Engl J Med 2014;370:1287–97.
30. Heigh RI, Yab TC, Taylor WR, et al. Detection of colorectal serrated polyps by stool DNA testing: comparison with fecal immunochemical testing for occult blood (FIT). PLoS One 2014;9:e85659.
31. Song LL, Li YM. Current noninvasive tests for colorectal cancer screening: An overview of colorectal cancer screening tests. World J Gastrointest Oncol 2016;8:793–800.
32. Pickhardt PJ, Hassan C, Halligan S, et al. Colorectal cancer: CT colonography and colonoscopy for detection—systemic review and meta-analysis. Radiology 2011;259:393–405.
33. Weinberg DS, Pickhardt PJ, Bruining DH, et al. Computed tomography colonography vs colonoscopy for colorectal cancer surveillance after surgery. Gastroenterology 2018;154:927–34.
34. Duarte RB, Bernardo WM, Sakai CM, et al. Computed tomography colonography versus colonoscopy for the diagnosis of colorectal cancer: a systemic review and meta-analysis. Ther Clin Risk Manag 2018;14:349–60.
35. Rex DK, Adler SN, Aisenberg J, et al. Accuracy of capsule colonoscopy in detecting colorectal polyps in a screening population. Gastroenterology 2015; 148:948–57.
36. Hariharan R, Jenkins M. Utility of the methylated SEPT9 test for the early detection of colorectal cancer: a systematic review and meta-analysis of diagnostic test accuracy. BMJ Open Gastroenterol 2020;7:e000355.
37. American Cancer Society Guideline for Colorectal Cancer Screening. American Cancer Society. Available at: https://www.cancer.org/cancer/colon-rectal-cancer/detection-diagnosis-staging/acs-recommendations.html. Accessed April 2, 2020.
38. United States Preventive Services Task Force. Screening for Colorectal Cancer. US Preventive Services Task Force Recommendation Statement. JAMA 2016; 315(23):2564–75.
39. American Gastroenterological Association. Statement from the U.S. Multisociety Task Force on Colorectal Cancer. 2018. Available at: https://www.gastro.org/press-release/statement-from-the-u-s-multisociety-task-force-on-colorectal-cancer. Accessed May 5, 2020.
40. National Colorectal Cancer Roundtable. Colorectal Cancer Screening Rates. Available at: https://nccrt.org/data-progress/#:~:text=The%20UDS%20CRC%

20screening%20rate,exceeded%20an%2080%25%20screening%20rate. Accessed June 1, 2020.
41. National Colorectal Cancer Round Table. Colorectal cancer screening data set update: how are we doing on our efforts to reach 80%?. 2019. Available at: https://nccrt.org/resource/colorectal-cancer-screening-data-set-update-how-are-we-doing-on-our-efforts-to-reach-80-january-28-2019/. Accessed June 1, 2020.
42. Escoffery C, Fernandez ME, Vernon SW, et al. Patient navigation in a colorectal cancer screening program. J Public Health Manag Pract 2015;21:433–40.
43. Howard DH, Guy GP, Ekwueme DU. Eliminating cost-sharing requirements for colon cancer screening in medicare. Cancer 2014;120:3850–2.
44. Removing Barriers to Colorectal Screening Act of 2015, H.R. 1220, 114th Congress 2015. Print.
45. SCREEN Act of 2015, H.R. 2035, 114th Congress 2015. Print.