American College of Radiology ACR Appropriateness Criteria[®] Colorectal Cancer Screening

Variant 1:

Colorectal cancer screening. Average-risk individual. Age greater than or equal to 50 years. Initial screening, then follow-up every 5 years after initial negative screen.

Procedure	Appropriateness Category	Relative Radiation Level
CT colonography	Usually Appropriate	\$ \$ \$
X-ray barium enema double-contrast	May Be Appropriate	\$ \$ \$
MR colonography	May Be Appropriate	0
X-ray barium enema single-contrast	Usually Not Appropriate	\$ \$ \$

Variant 2:

Colorectal cancer screening. Moderate-risk individual. First-degree family history of cancer or adenoma. Initial screening, then follow-up every 5 years after initial negative screen.

Procedure	Appropriateness Category	Relative Radiation Level
CT colonography	Usually Appropriate	* * *
X-ray barium enema double-contrast	May Be Appropriate	\$ \$ \$
MR colonography	May Be Appropriate	0
X-ray barium enema single-contrast	Usually Not Appropriate	\$ \$ \$

Variant 3:

Colorectal cancer detection. Moderate-risk individual. Average-risk individual after positive fecal occult blood test (FOBT) or positive fecal immunochemical test indicating a relative elevation in risk.

Procedure	Appropriateness Category	Relative Radiation Level
CT colonography	Usually Appropriate	\$ \$ \$
X-ray barium enema double-contrast	May Be Appropriate	\$ \$ \$
MR colonography	May Be Appropriate	0
X-ray barium enema single-contrast	Usually Not Appropriate	\$ \$ \$

<u>Variant 4:</u> Colorectal cancer screening. High-risk individual. Hereditary nonpolyposis colorectal cancer; ulcerative colitis or Crohn colitis.

Procedure	Appropriateness Category	Relative Radiation Level
CT colonography	Usually Not Appropriate	\$ \$ \$
MR colonography	Usually Not Appropriate	0
X-ray barium enema double-contrast	Usually Not Appropriate	\$ \$ \$
X-ray barium enema single-contrast	Usually Not Appropriate	\$ \$ \$

<u>Variant 5:</u> Colorectal cancer screening. Average-, moderate-, or high-risk individual after incomplete colonoscopy.

Procedure	Appropriateness Category	Relative Radiation Level
CT colonography	Usually Appropriate	* * *
X-ray barium enema double-contrast	May Be Appropriate	\$ \$ \$
MR colonography	Usually Not Appropriate	0
X-ray barium enema single-contrast	Usually Not Appropriate	\$ \$ \$

COLORECTAL CANCER SCREENING

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Summary of Literature Review

Introduction/Background

Colorectal cancer is the second leading cause of cancer death in the United States [1]. An average-risk individual has an approximately 4% to 5% lifetime risk of developing colorectal cancer [2]. Screening can prevent colorectal cancer by identifying benign precursor lesions and improve outcomes by detecting asymptomatic early-stage cancers. Large randomized clinical trials (>400,000 participants studied over decades in some studies) have shown decreased colorectal cancer-specific mortality compared with no screening (incidence rate ratio 0.73; 95% CI, 0.66–0.82) [3-12]. Results from case-control studies have suggested a protective effect lasting 5 to 10 years after direct structural examination of the colon [13,14].

Evidence has accumulated to support the concept that the majority of colorectal cancers develop from benign polyps of an adenomatous histology and that, in most cases, this transformation process is slow, requiring an average of 10 years [15,16]. More recently, a second pathway, mediated through benign hyperplastic or serrated polyps, has been identified, accounting for 20% to 25% of sporadic cancers [17]. The serrated polyp pathway is purported to also have a long dwell time [17-19]. Most colonic polyps are diminutive (<5 mm) in size with a much smaller percentage of small (6–9 mm) polyps. Large polyps (\geq 10 mm) constitute only 4% to 5% of polyps [20].

The rate of carcinoma and high-grade dysplasia is very low or low in subcentimeter adenomas, reported at 0.05% in diminutive polyps and 0.9% in 6- to 9-mm polyps [21]. In larger adenomas measuring 10 to 20 mm in size, the rate begins to increase to 7.3% [21]. Over time, only a very small minority of all adenomas ultimately progress to cancer. The majority of polyps remain stable or regress over time [22,23]. On the other hand, adenomas >25 mm have a 22.5% chance of containing invasive cancer or high-grade dysplasia [21]; polyps \geq 10 mm have an 8% chance of progressing to invasive cancer at 10 years, which increases to 24% at 20 years [24].

A number of organizations have issued recommendations for colorectal cancer screening, which are presented as lists of options. Recommendations for average-risk individuals from the United States Preventative Services Task Force include either colonoscopy every 10 years, computed tomographic colonography (CTC) every 5 years, or a stool-based test every 1 to 3 years, depending on the sensitivity of the stool-based test [25]. In addition to these options, the American Cancer Society (ACS) also includes double-contrast barium enema (DCBE) every 5 years in its list of recommended screening tests [26]. The ACS guidelines also separate colorectal cancer screening tools into 2 categories: 1) those that can screen for both adenomatous polyps and cancer (CTC, colonoscopy, and DCBE); and 2) those that are intended to screen for cancer only (fecal occult blood test [FOBT], fecal immunochemical test, and stool DNA test) [26]. The ACS recommends that tests that simultaneously screen for polyps and cancers should be preferred over tests that detect cancers only when resources permit [26].

A joint guideline from the ACS, the U.S. Multi-Society Task Force on Colorectal Cancer, and the ACR [27] has divided colorectal cancer risk levels into 3 categories: 1) average risk (individuals \geq 50 years of age), 2) moderate risk (individuals with a personal history of a large adenoma or carcinoma or a first-degree relative with a history

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of adenoma or carcinoma), and 3) high risk (individuals with hereditary syndromes, such as hereditary nonpolyposis colorectal cancer (HNPCC), or a personal history of ulcerative colitis or Crohn colitis).

Special Imaging Considerations

Regarding CTC, adherence to the ACR practice parameter for performing CTC in adults is important for optimal test performance and should reduce the variability reported in earlier CTC studies [28]. For screening, a standard protocol should involve catharsis and tagging. If alternative cathartic-free approaches are utilized, limitations should be highlighted. Automated carbon dioxide insufflation is preferred as this leads to consistently optimal distention as opposed to manual room air insufflation. Thin-slice thickness with a multidetector scanner to allow short reasonable breath holds is recommended. This guideline reinforces a 6-mm threshold for polyps where diminutive (\leq 5 mm) polyps are not reported given their likely lack of clinical significance. Nonreporting of diminutive lesions places these polyps essentially in 5-year follow-up (ie, the routine screen interval). The very few diminutive polyps that matter should grow over this period and can be identified at this later date. A strength of CTC is the size threshold and only removing higher risk lesions versus removing all diminutive lesions, thereby decreasing resource utilization and decreasing procedure-related complications by selectively doing polypectomies [29].

The ACR practice parameter also includes suggestions regarding the interpretation and reporting of extracolonic findings [28]. To avoid unnecessary further workup and patient anxiety, caution is emphasized when reporting findings that are likely to be of low clinical significance. There is evidence that using structured reporting constructs, such as CT Colonography Reporting and Data System, can decrease workups related to incidental extracolonic findings to <10% [30-32]. Unsuspected extracolonic malignancies and previously unknown aortic aneurysms are detected with CTC examinations in approximately 2% to 3% of patients [30,31,33-36].

Regarding barium enema, as utilization of DCBE has declined, training in this modality has also decreased [37], and it is not known if the barium enema data collected from studies performed by radiologists with extensive experience in the technique can be extrapolated to radiologists with lesser experience. For this document, it is assumed procedures are performed and interpreted by experts.

Discussion of Procedures by Variant

Variant 1: Colorectal cancer screening. Average-risk individual. Age greater than or equal to 50 years. Initial screening, then follow-up every 5 years after initial negative screen.

CTC

CTC (also known as "virtual colonoscopy") was introduced in 1994 as a less invasive method of imaging the colon by using helical CT. Similar to optical colonoscopy; patients undergo a preprocedural bowel cleansing preparation though with the addition of stool and fluid tagging agents. CTC is a considerably less invasive test as compared to optical colonoscopy, as reflected in the complication rate, in which the rate of perforation is 1 in 22,000 for CTC as opposed to 1 in 1,000 for diagnostic colonoscopy [38,39]. The rectal tube is only inserted a short distance into the rectum to perform CTC, whereas the colonoscope traverses the entire length of the colon at colonoscopy. Additionally, CTC is performed without sedation, thus foregoing any complications associated with sedation.

The American College of Radiology Imaging Network (ACRIN) National CTC Trial is the largest U.S. multicenter trial to date [40]. Fifteen sites recruited a total of 2,531 asymptomatic patients, who underwent multidetector-row CTC (16 rows or more) with stool and fluid tagging and mechanical carbon dioxide insufflation of the colon. All participating radiologists had to complete a qualifying examination, with a minimum accuracy of 90% for large polyps. Per-patient sensitivity, specificity, and positive and negative predictive values were 90%, 86%, 23%, and 99%, respectively, for detecting \geq 10-mm adenomas or cancers. The per-patient sensitivity for detecting adenomas \geq 6 mm was 78%. The per-polyp sensitivity for \geq 10-mm adenomas or cancers was 84%. When comparing primary 2-D and primary 3-D interpretation methods, no difference in sensitivity was identified for the detection of large polyps.

In another large study of 1,233 asymptomatic average-risk individuals undergoing colorectal cancer screening, the sensitivities of CTC and colonoscopy for detecting adenomatous polyps ≥ 10 mm were 94% and 88%, respectively [41]. A trial performed with 307 asymptomatic subjects using 64 multidetector-row CT demonstrated a CTC sensitivity and specificity of 91% and 93%, respectively, for polyps ≥ 6 mm and 92% and 98%, respectively, for polyps ≥ 10 mm [42]. Two meta-analyses of CTC performance in detecting ≥ 10 -mm polyps showed pooled

sensitivities by patient of 85% and 93%, with pooled specificities of 97% [43,44]. Some older studies have shown poorer performance of CTC (sensitivity of 55% to 59%) [45,46]. These discrepant results were likely related to differences in study design, lack of reader training, and CTC technique (eg, no fecal tagging) in these older studies.

The diagnostic yields of CTC and colonoscopy for advanced neoplasia have also been compared in parallel screening programs [47]. Primary CTC screening in 3,120 patients was compared with primary colonoscopy screening in 3,163 subjects. Similar detection rates were found for CTC and colonoscopy screening, which identified 123 and 121 advanced neoplasms, respectively. The referral rate for colonoscopy in the CTC group was 8%. The total numbers of polyps removed in the CTC and colonoscopy groups were 561 and 2,434, respectively. Seven perforations occurred in the colonoscopy group, but there were none in the CTC group. A multi-center randomized trial of 1,610 patients assigned to undergo either colonoscopy (n = 1,072) or CTC (n = 538) found an 11% detection rate for cancers and polyps \geq 10 mm with both techniques [48].

A review of a 1-year CTC screening experience for colorectal neoplasia showed that 3.9% of individuals had 1 polyp \geq 1 cm, and 6.9% had \geq 1 polyp(s) 6 to 9 mm [20]. Of the 71 patients who chose colonoscopy for further evaluation of these polyps, concordant lesions were found with colonoscopy in 65 (91.5% positive predictive value) [20]. In addition, the outcomes of patients with negative CTC screens have also been reported. A longitudinal follow-up of 1,011 patients over nearly 5 years demonstrated a single-interval cancer (crude cancer incidence of 0.2 cancers per 1,000 patient years), leading to the conclusion that a 5-year routine screen interval and nonreporting of diminutive lesions (\leq 5 mm) were appropriate strategies [49].

CTC performance has been evaluated in senior patient cohorts (\geq 65 years of age). A retrospective analysis of 577 subjects found an excellent CTC concordance rate of 91% [50]. Based on a 6-mm threshold, there was an overall patient referral rate of 15% for colonoscopy. Considering only adenomas, the per-patient positivity rates for 6- and 10-mm thresholds were 11% and 7%, respectively. When comparing 204 nonsenior (14%) and 250 senior patients (13%) undergoing CTC, another study found no statistically significant difference in the percentage of individuals with at least 1 polyp \geq 6 mm [51]. A post hoc analysis of 477 senior patients from the ACRIN National CTC Trial demonstrated that for large neoplasms, sensitivity and specificity among the older cohort were 82% and 83%, respectively [52]. There was no statistically significant difference when compared with the sensitivity and specificity of 92% and 86%, respectively, for lesions \geq 10 mm in the younger patient cohort. For lesions >6 mm, the sensitivity and specificity were 72% and 86%, respectively, for older patients and 81% and 89%, respectively, for younger patients, with no statistically significant difference. Another study reporting outcomes of 1,400 senior patients who underwent CTC found a 15% frequency for referral to colonoscopy at a polyp threshold of 6 mm [53]. Colorectal neoplasia was identified in 9% of patients, and advanced neoplasia was found in 3%.

Similar to colonoscopy, evidence supporting serrated polyp detection at CT is emerging. Despite a subtle, flat nature to sessile serrated polyps, these lesions can be detected at CTC likely because of a phenomenon of polyp coating. It appears that the adherent mucin elaborated by these lesions mix with the tagging agents to form a contrast coat. In an observational CTC screening study (n = 8,289), CTC demonstrated a prevalence of 3.1% for serrated lesions ≥ 6 mm in size. As seen by the colonoscopy experience, these lesions tended to be large (>10 mm in size), flat, and right sided. The presence of a contrast coat markedly improved lesion detection with an odds ratio of 40.4 (95% CI, 10.1, 161.4) [54].

Noncathartic CTC also has been assessed in recent years and does not perform as well as conventional CTC. In a prospective study of 605 adults at average to moderate risk for colon cancer who underwent both laxative-free CTC and colonoscopy, per patient sensitivity and specificity of CTC were 91% and 85% for adenomas \geq 10 mm, 70% and 86% for adenomas \geq 8 mm, and 59% and 88% for adenomas \geq 6 mm [32]. In a prospective study of 564 asymptomatic adults who underwent noncathartic CTC with fecal tagging, the sensitivity, specificity, negative predictive value, and positive predictive value of noncathartic CTC for adenomatous polyps or cancer \geq 6 mm were 76%, 92%, 98%, and 38%, respectively [55].

DCBE

DCBE also requires a preprocedural bowel cleansing preparation. The study is performed by administration of a liquid barium-based contrast agent and air-insufflation of the colon via a tube inserted into the rectum. Images are acquired with the patient in different obliquities and at different table angulations ranging from supine to standing. Performance of DCBE is dependent on optimal patient positioning because patient anatomy varies. The

perforation rate during DCBE is approximately 1 in 25,000 [56] as compared to 1 in 22,000 for CTC and 1 in 1,000 for diagnostic colonoscopy [38,39].

The best evidence regarding the performance of DCBE comes from studies in which patients underwent both DCBE and endoscopy. In a prospective trial including 614 patients, each of whom underwent DCBE and colonoscopy, per-patient sensitivity and specificity of DCBE were 48% and 90%, respectively, for lesions ≥ 10 mm and 41% and 82% for lesions ≥ 6 mm, respectively [46]. In an evaluation of 190 patients who underwent DCBE and colonoscopy, overall sensitivity for polyps was 70%, which increased to 80% for polyps >10 mm [57]. In an evaluation of 675 patients who underwent both flexible sigmoidoscopy and DCBE, DCBE missed 35% of polyps 6 to 10 mm and 17% of polyps >11 mm [58].

A retrospective study evaluated the diagnostic yield of DCBE examinations performed for colorectal cancer screening in average-risk individuals >50 years of age [59]. The diagnostic yield was 5.1% for neoplastic lesions \geq 10 mm and 6.2% for advanced neoplastic lesions, regardless of size. These diagnostic yields fall within the lower range of those reported for screening colonoscopy (5.0% to 9.5% for colonic neoplasms \geq 10 mm [60-62] and 4.6% to 11.7% for advanced colonic neoplasms, regardless of size [60,62,63]).

Additional data on the effectiveness of the DCBE for detecting colorectal cancer comes from studies in which the imaging history of patients with colorectal cancer was reviewed. In many of these studies, the risk level of patients undergoing DCBE was not reported. Based on this methodology, the sensitivity of DCBE ranges from 75% to 95% [64-66]. This correlates with a large, population-based study that found the overall rate of new or missed cancers following a DCBE was 22% [67].

A meta-analysis comparing the performance of the DCBE with CTC for detecting polyps ≥ 6 mm included 11 studies using DCBE (5,995 patients, 1,548 polyps) and 30 studies using CTC (6,573 patients, 2,348 polyps) [68]. Despite the inclusion of CTC studies with older techniques, statistically lower sensitivity and specificity were still seen for the DCBE compared with CTC.

SCBE

Single-contrast barium enema (SCBE) studies are performed by administration of liquid barium via a rectal tube. Unlike a DCBE, the colon is not insufflated with air. SCBE studies are generally performed when patients are unable to tolerate a DCBE (eg, patients unable to stand upright) and a CTC cannot be performed.

A preponderance of the literature has demonstrated a markedly inferior performance profile for SCBE. A retrospective evaluation of 139 patients who underwent barium enema and had 1 or more colonic polyps diagnosed endoscopically found sensitivity of SCBE for polyps <1 cm to be 72% and for polyps \geq 1 cm to be 94% [69]. In the same study, the sensitivity of DCBE was 88% for polyps <1 cm and 96% for polyps \geq 1 cm [69]. Patient risk level was not reported in this study.

A minority of studies have suggested that a SCBE has the potential to be as sensitive as a DCBE for detecting cancer and large polyps. The reported sensitivity for cancer ranges from 82% to 95% [65,66] and is approximately 95% for large polyps [69]. In a retrospective evaluation of individuals diagnosed with colorectal cancer who had undergone a prior DCBE or SCBE, the cancer miss rate was 4.8% for SCBE and 4.7% for DCBE [65]. However, because of the paucity of studies and limitations of the study designs, questions have been raised about the reproducibility of the results, particularly for large polyps.

MR Colonography

Magnetic resonance (MR) colonography for colorectal cancer screening is generally considered an investigational test in the United States and has not been adequately validated as an acceptable test for colorectal cancer screening. Although high-resolution imaging is possible with MR techniques, acquisition times are longer as compared to CT imaging, leading to a tradeoff between high resolution and long acquisition time (with resultant motion degradation) with currently available technology. Optimal technique is a source of active investigation, and distention of the colon with liquid (a diluted gadolinium solution for "bright lumen" T1-weighted imaging [70,71] or tap water for "dark lumen" T1-weighted imaging [72,73]), air insufflation without bowel cleansing [74], and administration of intravenous contrast material have been evaluated [75].

With current techniques, MR colonography does not perform as well as CTC for detection of polyps, especially for small lesions. Fewer published studies are available evaluating MR colonography as compared to CTC, and sample sizes are generally small for MR colonography studies, which remains primarily an investigational technique. In a systematic review of 13 prospective studies evaluating MR colonography performance in 1,285

patients, including asymptomatic patients at average risk and symptomatic patients at increased risk, the perpatient sensitivity and specificity for polyps ≥ 10 mm were 88% and 99%, respectively [76]. On a per-polyp basis, polyps of >10 mm were detected with a sensitivity of 84%. The data were found to be too heterogeneous for diminutive polyps <6 mm and for small polyps measuring 6 to 9 mm.

In a study of 286 asymptomatic individuals who underwent both 3T MR colonography and colonoscopy on the same day, sensitivity and specificity of MR colonography for adenomas ≥ 6 mm were 78% and 95%, respectively [77]. In an evaluation of 46 patients (screening and asymptomatic) who underwent MR colonography followed by colonoscopy, MR colonography was 67% sensitive and 96% specific for polyp detection on a per-patient basis [75] and was 100% sensitive (4/4) and 100% specific (20/20) for lesions 6 to 9 mm [75]. In a smaller pilot study of 29 patients who underwent both MR colonography performed with barium fecal tagging and air distention followed by colonoscopy, for ≥ 10 -mm lesions, the sensitivity and specificity of MR colonography were 44 and 100%, respectively. However, for 5- to 9-mm lesions, specificity was 95% but sensitivity was only 6% [74]. The risk level of patients was not reported.

Variant 2: Colorectal cancer screening. Moderate-risk individual. First-degree family history of cancer or adenoma. Initial screening, then follow-up every 5 years after initial negative screen.

CTC

Less evidence is available assessing the performance of CTC in moderate-risk as compared to average-risk individuals. In a study evaluating 156 asymptomatic individuals with a family history of colorectal cancer (defined as a first-degree relative [parent, sibling, or child] diagnosed with colorectal cancer before 60 years of age, or 2 first-degree relatives diagnosed with colorectal cancer at any age) and 8,857 subjects without family history of colorectal cancer, the referral rate for colonoscopy was higher in the family history cohort (16.0% versus 10.5%; P=0.035), but the frequencies of proven cancer (0.0% versus 0.4%), advanced adenoma (4.5%) versus 3.2%), and nonadvanced adenoma (5.1% versus 2.6%) were not significantly increased [78]. The results of this study suggest that CTC is a viable screening option for individuals at moderate risk due to family history.

DCBE

Limited evidence is available regarding the performance of DCBE in individuals with a family history of colorectal cancer. An older investigation of screening with colonoscopy or sigmoidoscopy and DCBE compared to no screening found a reduction in colorectal cancer incidence with screening in families with hereditary nonpolyposis colorectal cancer [79].

SCBE

SCBE generally does not perform as well as DCBE for detection of polyps and cancers and should be used if CTC or DCBE cannot be performed. Limited evidence is available regarding the performance of SCBE in individuals with a family history of colorectal cancer.

MR Colonography

Data regarding the performance of MR colonography in moderate-risk individuals is limited. In a study of 200 patients with a family or personal history of colorectal cancer or adenomatous polyps, per-patient sensitivity for polyps ≥ 10 mm was 58% to 67%, and per-patient specificity was 95% to 97% [80].

Variant 3: Colorectal cancer detection. Moderate-risk individual. Average-risk individual after positive fecal occult blood test (FOBT) or positive fecal immunochemical test indicating a relative elevation in risk. CTC

CTC also performs well in individuals with positive stool-based screening tests. A meta-analysis of 5 articles published between 2009 and 2011 showed that CTC had a per-patient sensitivity of 88.8% (95% CI, 83.6% to 92.5%) for ≥6-mm adenomas or colorectal cancer with average specificity of 75.4% (95% CI, 58.6% to 86.8%) for a pooled study population of 622 patients with positive FOBTs either by guaiac or immunochemical methods [81]. This was despite the fact that 2 of the 5 studies in the meta-analysis utilized a cathartic-free approach, which is known to decrease adenoma detection. Fecal tagging was variably used, which may have contributed to the relatively lower specificity [81]. In this meta-analysis, the calculated prevalence for >6-mm adenomas or cancer ranged from 32.0% to 65.3%, leading the authors to suggest that colonoscopy should likely remain the preferred test for FOBT-positive patients when feasible [81]. If rates are truly elevated in this range, this would certainly decrease the usefulness of CTC in this scenario where too many individuals would be referred on to colonoscopy. However, it is important to realize that evidence exists that these rates are much lower. A larger observational study (n = 2,731) reported CTC use in FOBT-positive patients within the English Bowel Cancer Screening Program. Here, the prevalence for FOBT-positive group was 23.4% for a polyp ≥ 6 mm in size [82]. If the prevalence is more in this range, referral rates from CTC would then be reasonable and allow a CTC-based strategy to decrease numbers of unnecessary nontherapeutic colonoscopies. There is currently no evidence to support or to not support the use of CTC following a positive stool DNA test.

DCBE

In symptomatic patients (eg, rectal bleeding, abdominal pain, weight loss), DCBE was found to detect fewer cancers or polyps ≥ 10 mm as compared to CTC in a pragmatic multicenter randomized trial of 3,506 symptomatic patients [83]. In a smaller, older study of 154 patients presenting with symptoms and subsequently diagnosed with colorectal carcinoma, DCBE was found to detect 64% of colorectal cancers [84]. DCBE was found to have a sensitivity of 85% for the diagnosis of colorectal cancer in 485 patients, the majority of whom were symptomatic [66].

In studies comparing DCBE to endoscopy, when used to evaluate individuals with a positive FOBT, most reports indicate a sensitivity of 75% to 80% [85,86]. In a study comparing DCBE to endoscopy in 71 patients with rectal bleeding, the sensitivity of DCBE for detecting adenomas >6 mm was 58% [87].

SCBE

SCBE generally does not perform as well as DCBE for detection of polyps and cancers and should be used if CTC or DCBE cannot be performed. In a retrospective evaluation of 165 patients who underwent SCBE, the sensitivity for colorectal cancer was 81.8% [66]. The majority of these patients were symptomatic (eg, bleeding, anemia, altered bowel habit) at time of imaging [66]. In a FOBT trial, SCBE was used as a diagnostic follow-up and the sensitivity for cancer was 80% [88].

MR Colonography

Data regarding the performance of MR colonography in moderate-risk individuals is limited. In a 3-reader study of 98 symptomatic patients (eg, rectal bleeding, change in bowel habits) who underwent both MR colonography with fecal tagging and CO₂ insufflation and colonoscopy, per-patient sensitivity for lesions ≥ 10 mm ranged from 75% to 92% across the 3 readers with specificity ranging from 95% to 98% [89]. Per-patient sensitivity for lesions ≥ 6 mm ranged from 57% to 86% and specificity ranged from 87% to 99%. For advanced neoplasia ≥ 6 mm, per-patient sensitivity was 89% and specificity ranged from 97% to 99% [89]. In a study of 24 patients who presented with rectal bleeding, a positive FOBT, or altered bowel habits, MR colonography with barium-based fecal tagging detected all polyps >8 mm [90]. A tap water enema was used to distend the colon, and intravenous contrast material was administered [90].

Variant 4: Colorectal cancer screening. High-risk individual. Hereditary nonpolyposis colorectal cancer; ulcerative colitis or Crohn colitis.

The risk of cancer in individuals with ulcerative colitis increases after the disease has been present 8 to 10 years, and it correlates with the extent of the disease. The cumulative probability of colorectal cancer in an ulcerative colitis patient is 2% by 10 years, 8% by 20 years, and 18% by 30 years [91]. The risk for individuals with Crohn colitis may be comparable. Unlike the other forms of colorectal cancer screening, the screening of ulcerative colitis patients focuses on detecting dysplasia (which may be flat and identified only by random biopsies, or it may be macroscopically visible) and a subsequent prophylactic colectomy. There is no evidence of a reduction in mortality resulting from colorectal cancer screening in these patients, although annual colonoscopy screening has demonstrated a shift to early-stage detection. For patients at high risk because of known ulcerative colitis or Crohn colitis, a colonoscopy is preferred over CTC, MR imaging, or barium examinations because of its ability to obtain biopsies to look for dysplasia.

Individuals with HNPCC, also known as Lynch syndrome, are at increased risk for colorectal cancer. Colorectal cancers tend to occur at a younger age and with a shorter dwell time in individuals with HNPCC [92]. Colorectal cancer screening recommendations for individuals with HNPCC or at risk (first-degree relatives) are colonoscopy every 1 to 2 years beginning at 20 to 25 years of age or earlier if familial diagnosis of colorectal cancer before age 25 years [92].

СТС

Colonoscopy is preferred over CTC because of its ability to obtain biopsies to look for dysplasia.

DCBE

Colonoscopy is preferred over barium examinations because of its ability to obtain biopsies to look for dysplasia.

MR Colonography

Colonoscopy is preferred over MR imaging because of its ability to obtain biopsies to look for dysplasia.

SCBE

Colonoscopy is preferred over barium examinations because of its ability to obtain biopsies to look for dysplasia.

Variant 5: Colorectal cancer screening. Average-, moderate-, or high-risk individual after incomplete colonoscopy.

CTC

Several studies have demonstrated the usefulness of CTC in individuals who have undergone an incomplete colonoscopy [93-96]. In a study of 546 patients who underwent CTC after an incomplete colonoscopy, 13% were found to have lesions \geq 6 mm. Per-patient and per-lesion positive predictive values of CTC for masses and large polyps were 91% and 92%, respectively [97]. In a prospective study of 100 patients who underwent CTC after incomplete colonoscopy, CTC was found to have a positive predictive value of 86% and 100% for polyps \geq 6 mm and \geq 10 mm, respectively [98]. CTC following incomplete colonoscopy detected colorectal cancer in 9% and adenomatous polyps in 20% [99]. Performing a dedicated CTC bowel preparation on a later date following incomplete colonoscopy results in much higher examination quality compared to same-day CTC [100]. If same-day CTC is performed following incomplete colonoscopy, the patient should ingest a fecal tagging agent (eg, 30 mL oral diatrizoate) after recovery from sedation with imaging performed at least 2 hours after ingestion [100].

DCBE

Limited data have been published on the accuracy of DCBE following incomplete colonoscopy. In a study of 233 patients who underwent DCBE following incomplete colonoscopy, polyps were reported in 2.1% of patients (5 patients; 5 of 6 polyps >5 mm) [101]. However, 2 patients with 4- and 10-mm polyps reported on DCBE underwent repeat colonoscopy, and no polyps were found. The remaining 3 patients with polyps reported on DCBE refused repeat colonoscopy. Thirteen patients whose DCBE studies were reported as of suboptimal quality underwent repeat colonoscopy, and 5 patients were found to have polyps (one 1-cm tubular adenoma, 4 <5-mm hyperplastic polyps). In a study of 103 patients who underwent DCBE performed immediately after incomplete colonoscopy, the entire colon was visualized in 94% of subjects [102]. Five malignant neoplasms (size not reported) were identified at DCBE [102].

SCBE

Very limited data are available regarding the accuracy of SCBE performed after incomplete colonoscopy. In a study of 118 patients who underwent barium enema following incomplete colonoscopy (103 double contrast, 15 single contrast), 2 polyps were found (4 and 5 mm) and removed at subsequent repeat colonoscopy [103]. Repeat colonoscopic findings were not available for the vast majority of study subjects [103].

MR Colonography

Data regarding the performance of MR colonography following incomplete colonoscopy are limited to a small series. In an evaluation of 14 patients who underwent MR colonography after incomplete colonoscopy followed by a completion colonoscopy after surgical treatment of the high-grade stenosis, 9/9 polyps [5–20 mm] identified at MR colonography were confirmed at completion colonoscopy, though 2 polyps 5 and 8 mm seen on the postoperative colonoscopy were not seen on MR colonography [104].

Summary of Recommendations

- For average-risk individuals, CT colonography is usually appropriate for colorectal cancer screening.
- For moderate-risk individuals (eg, first-degree family history of cancer or adenoma), CT colonography is usually appropriate for colorectal cancer screening.
- For moderate-risk individuals after positive FOBT or positive fecal immunochemical test, CT colonography is usually appropriate for colorectal cancer detection.
- For high-risk individuals (eg, hereditary nonpolyposis colorectal cancer, ulcerative colitis, or Crohn colitis), colonoscopy is preferred over imaging tests because of its ability to obtain biopsies to look for dysplasia.
- For colorectal cancer screening after incomplete colonoscopy, CT colonography is usually appropriate for individuals at average, moderate, or high risk for colorectal cancer.

Summary of Evidence

Of the 105 references cited in the *ACR Appropriateness Criteria*[®] *Colorectal Cancer Screening* document, 98 references are categorized as diagnostic references including 12 well-designed studies, 16 good-quality studies, and 28 quality studies that may have design limitations. There are 42 references that may not be useful as primary evidence. There are 7 good quality references that are meta-analysis studies.

The 105 references cited in the ACR Appropriateness Criteria[®] Colorectal Cancer Screening document were published from 1983-2017.

Although there are references that report on studies with design limitations, 28 well-designed or good-quality studies provide good evidence.

Appropriateness Category Name	Appropriateness Rating	Appropriateness Category Definition
Usually Appropriate	7, 8, or 9	The imaging procedure or treatment is indicated in the specified clinical scenarios at a favorable risk- benefit ratio for patients.
May Be Appropriate	4, 5, or 6	The imaging procedure or treatment may be indicated in the specified clinical scenarios as an alternative to imaging procedures or treatments with a more favorable risk-benefit ratio, or the risk-benefit ratio for patients is equivocal.
May Be Appropriate (Disagreement)	5	The individual ratings are too dispersed from the panel median. The different label provides transparency regarding the panel's recommendation. "May be appropriate" is the rating category and a rating of 5 is assigned.
Usually Not Appropriate	1, 2, or 3	The imaging procedure or treatment is unlikely to be indicated in the specified clinical scenarios, or the risk-benefit ratio for patients is likely to be unfavorable.

Appropriateness Category Names and Definitions

Relative Radiation Level Information

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level (RRL) indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Patients in the pediatric age group are at inherently higher risk from exposure, both because of organ sensitivity and longer life expectancy (relevant to the long latency that appears to accompany radiation exposure). For these reasons, the RRL dose estimate ranges for pediatric examinations are lower as compared to those specified for adults (see Table below). Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria[®] Radiation Dose Assessment Introduction document [105].

Relative Radiation Level Designations		
Relative Radiation Level*	Adult Effective Dose Estimate Range	Pediatric Effective Dose Estimate Range
0	0 mSv	0 mSv
•	<0.1 mSv	<0.03 mSv
&	0.1-1 mSv	0.03-0.3 mSv
\$\$ \$\$	1-10 mSv	0.3-3 mSv
* * *	10-30 mSv	3-10 mSv
\$ \$ \$ \$ \$	30-100 mSv	10-30 mSv

*RRL assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (eg, region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as "Varies".

Supporting Documents

For additional information on the Appropriateness Criteria methodology and other supporting documents go to <u>www.acr.org/ac</u>.

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The ACR Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the FDA have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.