Health Technology Assessment

Appendix

Computed Tomographic Colonography (CTC)

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Presented by:

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1. ICER REVIEW PROTOCOL

Protocol for Systematic Review
Computed tomographic colonography versus optical colonoscopy

Objectives

The objective of this comparative effectiveness review is to assess the effectiveness and safety of computer tomographic (CT) colonography with that of traditional endoscopic colonoscopy for screening for the presence or absence of colorectal cancerous or precancerous lesions.

Specific questions to be addressed are:

1. What are the results and conclusions of currently available health technology assessments related to CT colonography?
2. What is the sensitivity and specificity of CT colonography compared with optical colonoscopy to detect one or more polyps or cancerous lesion per patient by lesion size (1 cm or more, 6 to 9 mm, 5 mm or less), during a single screening examination?
3. Do patients prefer CT colonography compared with other types of colorectal screening methods involving direct examination of the colon, or compared with fecal examination screening methods? Does preference change depending on whether the patient had previously experienced a CT colonography?
4. Is there an increase in patient compliance with current colorectal screening guidelines with the use of CT colonography as a screening method?
5. How do adverse events related to CT colonography compare with those related to optical colonoscopy, including but not limited to increased risk due to radiation, events related to false positive findings or extracolonic findings (e.g., increased costs of additional testing, anxiety, etc.), and bowel perforation.

Criteria for considering studies for this review

Types of studies

This review will include two types of studies. First, we will include all studies that prospectively compare the diagnostic performance of CT colonography with that of optical colonoscopy. Studies are eligible if a valid reference standard was used, and observers were kept unaware of colonoscopy results before evaluating the CT colonography findings. Studies are excluded if the study investigators did not collect data from which sensitivity and specificity could be determined.

Second, we will include studies that evaluate patient compliance, preference, or satisfaction with CT colonography compared with optical colonoscopy or another method of colorectal screening.

We will preferentially search for RCTs, but include all prospective study designs in our systematic review.

Types of participants

We will include trials in which the study population consisted of people who have agreed to undergo colorectal screening by CT colonography. Participants will be adults, classified by over and under 50, gender, or perceived risk for colorectal cancer (low risk or high risk). We will not include trials of colorectal cancer screening of individuals with Crohn's disease, irritable bowel syndrome, or a current or previous diagnosis of a gastrointestinal cancer.

Types of interventions

All types of CT colonography instrumentation and imaging technology will be considered for this review. The comparator for this review for the diagnostic specificity and sensitivity will be traditional endoscopic colonoscopy. The comparator for patient preference will be any method of colorectal cancer screening.

Types of outcome measures

The primary outcome of this review will be the sensitivity and specificity of CT colonography to detect a cancerous or pre-cancerous lesion (polyp) by patient by largest lesion size.
Secondary outcomes include the following:

- Sensitivity and specificity of CT colonography to detect a polyp 1 cm or more compared with that of optical colonoscopy;
- Sensitivity and specificity of CT colonography to detect a polyp between 6 to 9 mm compared with that of optical colonoscopy;
- Patient compliance with colorectal screening using CT colonoscopy compared with optical colonoscopy or other colorectal screening method;
- Patient preference for CT colonoscopy compared with optical colonoscopy or other colorectal screening method;
- Patient satisfaction with performance of CT colonoscopy compared with optical colonoscopy or other colorectal screening method;
- Adverse events related to CT colonography, including effect of increased radiation, events related to false positive or extracolonic findings, and rate of bowel perforation.

Identification of studies

Development of the search strategy

A search strategy will be developed by analyzing MEDLINE Medical Subject Headings (MeSH) headings used to analyzing the MEDLINE MeSH terms used to index key articles found in published meta-analyses. A preliminary analysis of 16 articles identified the following MeSH headings appearing in 4 or more articles:
colon/radiography
colonic polyps/radiography
colonography, computed tomographic
colonoscopy
colorectal neoplasms/diagnosis/radiography
image processing, computer-assisted
tomography, X-ray computed
sensitivity and specificity
predictive value of tests
prospective studies

These MeSH terms and text words related to the population, diagnostic tests, condition, and outcomes of interest will be incorporated into the final MEDLINE search strategy. Search filters (e.g., “adult”, “human, not animal”) will be applied when and if appropriate. The Cochrane Highly Sensitive Search Strategy will be used to identify RCTs and then modified to identify non-randomized, cohort, and case-control studies. Systematic reviews will be identified in MEDLINE by using the Publication Type index term [Meta-analysis] combined with appropriate MeSH and text word terms.

Electronic Searches

The search strategy will be used to search MEDLINE, documented the date of search. It will be modified for use in EMBASE, CENTRAL (the Cochrane database of controlled clinical trials found in *The Cochrane Library*), LILACS, and Science Citation Index. The search will include articles in any language.

We will also identify existing health technology assessments (HTAs) using a detailed documented search strategy. We will search the Health Technology Assessment database of *The Cochrane Library*, MEDLINE, and EMBASE for HTAs, documenting the date the search was conducted.

Other searches

We will also review references in identified HTAs, references found in systematic and other types of reviews and relevant papers, and references to identified studies found in Science Citation Index.

Methods of the review

Assessment of Current Health Technology Assessments

Full length copies of HTAs available through the internet will be obtained and conclusions of each HTA summarized.

Selection of studies for the review

Titles and abstracts of all articles identified by the electronic and manual searches will be assessed for compliance with eligibility criteria. The abstracts will be classified as definitely eligible, possibly eligible, or definitely ineligible. Full copies of those classified as definitely or possibly eligible will be obtained and re-assessed using the eligibility criteria. Final classification will be definitely eligible or definitely ineligible. Any study for which classification is not possible because of lack of information in the published report will be considered ineligible.

Classification of eligible articles by level of evidence

We will classify all identified eligible studies by the level of evidence, as follows:

Level I: randomized controlled trial;
Level II: quasi-randomized controlled trial (i.e., alternate allocations or some other method) or a comparative study with concurrent controls,
Level III: cohort studies, case-control studies or interrupted time series with a control arm;
Level IV: a comparative study without concurrent controls (historical controls study; 2 or more single arm studies; interrupted time series without a parallel control group
Level V: Case series with either post-test or pre-test/post-test outcomes.

Data extraction and management

The steps used to synthesize the available evidence include initial assessment of methodological quality and study characteristics followed by data abstraction, synthesis, and interpretation.

Assessment of methodological quality of included studies

For randomized trials, the following characteristics will be considered to be important for assessing validity of the trial: method used to assign study participants to treatment, allocation concealment, masking of outcome, and follow up. Each characteristic will be graded as adequate, inadequate, or unclear (or not reported) with grade documented on a data collection form. We will consider any study with inadequate allocation concealment to be of lower quality.

Bias in non-randomized studies will be assessed by scoring for selection bias, ascertainment bias, and comparability of treatment groups using the Newcastle Ottawa Quality Assessment Scale (NOS), a validated instrument developed by investigators from the Ottawa Health Research Institute and University of Newcastle, Australia (40).

Abstraction of Study Characteristics

We will extract data on study characteristics such as participant demographics, co-morbidities, and risk assessment; details of the technology; details of the outcomes measured; and other relevant information. Aspects of each study will be tabulated into an evidence table and used to inform the qualitative analyses and to evaluate the generalizability of the review results. In addition, we will specifically assess characteristics that have been documented as having an effect on measures of diagnostic test accuracy (Whiting 2004). These include:

- Demographic features of the test population
- Selection of the patient population;
- Disease severity
- Disease prevalence
- Verification of the index test results (partial verification, differential verification, or full verification)
- Test execution;
- Test technology;
- Clinical information available to the clinician interpreting the image; and
- Reader characteristics.

Data Synthesis

Preparation of Evidence Tables

The next step is the preparation of evidence tables. We will use a process similar to that developed by the GRADE group to evaluate the totality of evidence, not using those aspects related to intervention studies. The GRADE process takes into account the quality of evidence, the consistency of the evidence across all studies, and the directness of the evidence, defined as “the extent to which the people, interventions, and outcome measures are similar to those of interest.” The benefit and harm reported for each study will be assessed, and recorded in an evidence table along with the directness (applicability) of effect. The GRADE group also recommends assessing whether there was sparse data (SD), a strong association (SA), reporting bias (RB), a dose response effect (DR), and the application of all possible confounders (PC). These are graded as Yes or No. We will include these variables as applicable in the evidence table.

Investigation of heterogeneity

Sensitivity analysis

We will assess study design by the level of evidence, as described above, and then modify it by the quality assessment. For example, a randomized trial receives the highest ranking, but the rank will be decreased if the studies have methodological limitations that affect the validity of the results. We will rate overall study quality as having no serious limitations, serious limitations, or very serious limitations.

Other variables that we will explore are variations in instrument (e.g., single versus multi-detector), imaging (minimal collimation slice < 5 mm versus 5 mm or larger), software, and amount of observer training.

Interpretation

Data from the evidence table will be qualitatively summarized in a narrative review, taking into account confounding variables and other findings that affect the diagnostic characteristics of CT colonography.

2. PRELIMINARY REPORT OF ACRIN TRIAL RESULTS

ACRIN trial shows VC ready for widespread use

9/28/2007
By: Eric Barnes <mailto:ebarnes@auntminnie.com>

ARLINGTON, VA - Trial results unveiled today marked the apparent end of a long road to validation for virtual colonoscopy (VC or CT colonography [CTC]), a radiology-based colon screening exam whose advocates have toiled for more than a decade to show equivalent detection sensitivity in a large screening trial compared to more invasive optical colonoscopy.

Preliminary results of the National CT Colonography Trial (ACRIN 6664 <http://www.acrin.org/6664_protocol.html>), a study funded by the National Institutes of Health (NIH) and performed on 2,531 participants in 15 U.S. centers, yielded an impressive per-patient sensitivity of 90% for adenomatous colorectal lesions 1 cm or larger in diameter, a sensitivity on par with that of optical colonoscopy.

Optical colonoscopy retains the considerable advantage of being both diagnostic and therapeutic, in that colorectal polyps can be removed concurrently with their detection. Nevertheless, reported principal investigator Dr. C. Daniel Johnson from the Mayo Clinic in Rochester, MN, only 8.3% of trial participants would have proceeded to same-day optical colonoscopy for removal of polyps 6 mm or larger, a referral rate low enough to suggest that VC will not be too expensive an alternative for routine use in colorectal cancer screening. Inasmuch as optical colonoscopy served as a reference standard for the comparison of VC trial results, 100% of the participants were referred for the exam immediately after VC.

"Colon cancer is the second most common cancer killer in the U.S., affecting one in 18 individuals in the United States," Johnson said, adding the latest grim statistics: 145,290 new cases in 2007, and an estimated 73,470 deaths. Yet only one-third to one-half of the 70 million people eligible to screen in the U.S. ever get tested. It is hoped that the addition of a new alternative will encourage more individuals over 50 years of age to get screened, though as in optical colonoscopy, most VC patients will still have to undergo cathartic bowel cleansing before screening.

"From a patient perspective, once the colon's prepped, it's pretty easy, just two breath-holds in the prone and supine position, and then the examination is done on the image data rather than on the patient," said Johnson, a professor of radiology at the Mayo Medical School in Rochester, MN. He presented the first results of the trial at the 2007 ACRIN fall meeting.

The efficacy of colorectal cancer screening has already been proved because it can detect precursor lesions in the colon long before they progress to cancer, Johnson said. The problem with VC as a screening alternative has been the variability of multicenter trial results. While Pickhardt et al demonstrated 94% sensitivity and 96% sensitivity for significant colorectal lesions in more than 1,100 asymptomatic subjects in 2003, subsequent studies by Cotton et al and Rocky et al yielded sensitivities as low as 55% and 59%, respectively, for clinically significant polyps. These later results cast serious doubt on the robustness of VC as a screening method, though many radiologists maintained that poor study design and lack of training were the main problems.

"The aim of this (ACRIN) study was to evaluate the sensitivity of CT colonography for detecting participants with at least one adenoma a centimeter or larger using colonoscopy as the reference standard," Johnson said.

The 15 U.S. sites included both academic centers and private practices, which recruited 2,600 asymptomatic outpatients who were scheduled for optical colonoscopy screening. Those with symptoms suggestive of an elevated risk of colon cancer, such as blood in stool, abdominal pain, or family or personal history of colorectal polyps, were excluded from the study.

Training was an important component of the study, with VC readers obligated to have read at least 500 cases, or attend a 1.5-day training course. And all had to pass a certified exam in which they detected at least 90% of the adenomas 1 cm or larger in 50 cases, Johnson said.
CTC Appendix 02-01-08

"It's interesting to note that more than half of the readers had to undergo additional training in order to pass the certified exam initially, and with additional training, all the readers eventually passed," he said.

Stool tagging began 24 hours before imaging with the ingestion of 16 grams of barium sulfate in three doses with meals, Johnson said. This was followed the evening before VC with a cathartic prep and residual fluid tagging with 60 mL of a water-soluble iodinated contrast agent. All subjects received 1 mg of glucagon 10 minutes prior to mechanical colon insufflation with CO2.

After insufflation, prone and supine CT images were acquired on scanners representing each of the major vendors with a minimum of 16 detector rows. Thin-section images were acquired at 0.6-mm to 1.25-mm collimation with reconstructions at 0.8- to 1-mm intervals, using a low-dose protocol of 50 mAs. Colonoscopy was performed on the same day in 99% of the cases by experienced staff gastroenterologists, who were blinded to the VC results.

A central pathology laboratory examined the results of all polypectomies, and segmental unblinding of VC results for the gastroenterologists was not used. Lesion matching between the exams required each polyp detected at VC in the same segment and within 50% of the same size as detected at colonoscopy.

From a total of 2,600 subjects, eight were deemed ineligible, 10 withdrew from the study, 42 had incomplete colonoscopy, and nine had incomplete VC, leaving a total of 2,531 or slightly more than 97% of the total who completed the study, including 1,205 men and 1,362 women with an average age of 58 years, Johnson said. About 10% (n = 248) had an increased risk of colon polyps due to personal or family history of colon polyps, he said.

More than half of the studies were performed on 64-detector-row scanners, and were interpreted in either primary 2D or 3D reading on software from several major vendors.

Overall there were 547 polyps in 390 patients 5 mm or larger in size, 392 polyps 6-9 mm in 258 patients, and 155 lesions 1 cm or larger in 132 patients, Johnson said. The mean diameter was 8.9 mm, distributed fairly evenly between the right colon (29%), transverse colon (17%), left colon (38%), and rectum (16%).

A total of 374 of the 547 (68%) colonoscopy-proven lesions were adenomatous polyps or cancers, including 128 lesions 10 mm or larger in 109 patients (4.3%), and seven carcinomas 5 mm or larger in diameter, Johnson said.

The chart below shows VC's sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for detecting patients with adenomas ranging in size from 5 mm or larger to 10 mm or larger.

	= 5 mm	= 6 mm	= 7 mm	= 8 mm	= 9 mm	= 10 mm
Sensitivity	65%	78%	84%	87%	90%	90%
Specificity	89%	88%	87%	87%	86%	86%
PPV	45%	40%	35%	31%	25%	23%
NPV	95%	98%	99%	99%	99%	99%

"You can see that (VC) sensitivity remained high, 84% or more, for polyps 7 mm or larger," Johnson said. "Specificity remained high, 86% to 89%, across all lesions." The area under the curve rose from 80% to 90% for adenomas 5-10 mm in size.

Even the rigorous per-adenoma sensitivity measure was 59% (= 5 mm), 70% (= 6 mm), 75% (= 7 mm), 80% (= 8 mm), 82% (= 9 mm), and 84% (= 10 mm).

Interobserver variability was "actually quite tight," Johnson said, and seven of the 15 readers detected 100% of the polyps. Interestingly, the overall sensitivity difference between primary 2D reading (87%) and primary 3D reading (88%) was not statistically significant, he said. And 3D took almost six minutes longer to review on average, at 25.5 minutes versus 19.4 minutes for primary 2D. The various software packages used for interpretation did not yield significant differences in sensitivity either, Johnson added.

"I think we can say that CT colonography is similar to the performance of colonoscopy for large adenomas 1 cm or larger, as well as those intermediate adenomas 5-10 mm in diameter," Johnson said. "And I think it's reasonable to

consider broader application of this relatively noninvasive imaging modality, which hopefully will enhance compliance with colorectal cancer screening guidelines. The prevalence of those adenomas 6 mm or larger was 8.3%; this would indicate that most patients undergoing CT colonography wouldn't need colonoscopy, sparing them the cost, risk, and inconvenience of that second test."

The contributions of reader training and advanced techniques in the success of the trial cannot be underestimated, Johnson said. The success in the past has been attributed to the primary 3D reading technique, but the results showed that primary 2D can be as accurate. In addition, the study was performed with a low-dose CT technique yielding a total dose of about 5 mSv per exam, an amount the Health Physics Society considers a risk that is either nonexistent or "too small to be measured," he said.

Johnson said he expects the information to be of interest to the health agencies that define the tests that are included in colorectal screening guidelines, and called on the primary care and gastroenterology communities to work together with radiologists to prepare for the wider implementation of CT colonography for screening.

"I think the results show a remarkable amount of thoughtful effort" on the part of the researchers, commented Dr. Elizabeth McFarland, an associate professor of radiology at the Mallinckrodt Institute of Radiology at Washington University in St. Louis. What matters from this point forward is "how we disseminate this (modality) in a way that we maintain high standards and make it feasible for people to do out in the community," she said.

"Let's all agree that the validation phase is over, and let's work on widespread screening," commented Dr. Perry Pickhardt, an associate professor of radiology at the University of Wisconsin in Madison, in a telephone interview with AuntMinnie.com.

The 25-minute 3D reads "are almost triple our current reading times" using different software, added Pickhardt, a proponent of primary 3D reading. "But I'm not worried about the whole 2D/3D issue. People will find out on their own which method works best for them," he said. "The numbers are really good, and overall it's good news."

3. Reference: Polyp Size Threshold Article

(Follows on Next Page)

4. Prior Systematic Reviews

AHRQ Systematic Review (2002)

Canadian Center on HTA pre-assessment (2004)

Medical Services Advisory Committee, Australia (2006)

NICE, United Kingdom (2005)

Systematic Evidence Review
Number 7

Screening for Colorectal Cancer in Adults

Front Matter

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AHRQ is the lead Federal agency charged with supporting research designed to improve the quality of health care, reduce its cost, address patient safety and medical errors, and broaden access to essential services. AHRQ sponsors and conducts research that provides evidence-based information on health care outcomes; quality; and cost, use, and access. The information helps health care decisionmakers—patients and clinicians, health system leaders, and policymakers—make more informed decisions and improve the quality of health care services.

Systematic Evidence Review
Number 7

Screening for Colorectal Cancer In Adults

Prepared for:
Agency for Healthcare Research and Quality
U.S. Department of Health and Human Services
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Preface

The Agency for Healthcare Research and Quality (AHRQ) sponsors the development of Systematic Evidence Reviews (SERs) through its Evidence-based Practice Program. With guidance from the third U.S. Preventive Services Task Force* (USPSTF) and input from Federal partners and primary care specialty societies, two Evidence-based Practice Centers—one at the Oregon Health Sciences University and the other at Research Triangle Institute-University of North Carolina—systematically review the evidence of the effectiveness of a wide range of clinical preventive services, including screening, counseling, immunizations, and chemoprevention, in the primary care setting. The SERs—comprehensive reviews of the scientific evidence on the effectiveness of particular clinical preventive services—serve as the foundation for the recommendations of the third USPSTF, which provide age- and risk-factor-specific recommendations for the delivery of these services in the primary care setting. Details of the process of identifying and evaluating relevant scientific evidence are described in the "Methods" section of each SER.

The SERs document the evidence regarding the benefits, limitations, and cost-effectiveness of a broad range of clinical preventive services and will help to further awareness, delivery, and coverage of preventive care as an integral part of quality primary health care.

AHRQ also disseminates the SERs on the AHRQ Web site (http://www.ahrq.gov/uspstfix.htm) and disseminates summaries of the evidence (summaries of the SERs) and recommendations of the third USPSTF in print and on the Web. These are available through the AHRQ Web site (http://www.ahrgq.gov/uspstfix.htm), through the National Guideline Clearinghouse (http://www.ncg.gov), and in print through the AHRQ Publications Clearinghouse (1-800-358-9295).

We welcome written comments on this SER. Comments may be sent to: Director, Center for Practice and Technology Assessment, Agency for Healthcare Research and Quality, 6010 Executive Blvd., Suite 300, Rockville, MD 20852.

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* The USPSTF is an independent panel of experts in primary care and prevention first convened by the U.S. Public Health Service in 1984. The USPSTF systematically reviews the evidence on the effectiveness of providing clinical preventive services--including screening, counseling, immunization, and chemoprevention--in the primary care setting. AHRQ convened the third USPSTF in November 1998 to update existing Task Force recommendations and to address new topics.

The authors of this report are responsible for its content. Statements in the report should not be construed as endorsement by the Agency for Healthcare Research and Quality or the U.S. Department of Health and Human Services of a particular drug, device, test, treatment, or other clinical service.

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Figures

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Structured Abstract

Context: Colorectal cancer is an important cause of cancer-related morbidity and mortality in the United States. Screening has the potential to reduce the morbidity and mortality from colorectal cancer through early detection and removal of early-stage cancers or precancerous adenomatous polyps.

Objective: We conducted a systematic review for the US Preventive Services Task Force to assess the effectiveness and cost-effectiveness of different colorectal cancer screening tests.

Data sources: We used recently conducted systematic reviews, the second edition of the *Guide to Clinical Preventive Services*, the British National Health Service Economic Evaluation database, and focused searches of MEDLINE from 1966 through September 2000 to identify relevant studies for inclusion. We also conducted hand-searches, review of bibliographies, and consultations with context experts to assure completeness.

Study selection: When available, we included the most recent high-quality systematic review and then supplemented that review with a search for more recent articles. Full MEDLINE searches were performed to examine the accuracy of double-contrast barium enema, the rates of complications for each of the available screening tests, and for studies of the cost-effectiveness of screening. Two reviewers examined the results of each of the full searches and determined by consensus which articles should be abstracted into evidence tables.

Data extraction: One reviewer abstracted the information from the final set of studies into evidence tables, and a second reviewer checked them for accuracy.

Data synthesis: Direct evidence from multiple well-conducted randomized trials supports the effectiveness of fecal occult blood testing (FOBT) in decreasing colon cancer incidence and reducing mortality from colorectal cancer compared with no screening for average-risk adults over age 50. Data from well-conducted case-control studies support the effectiveness of sigmoidoscopy and possibly colonoscopy in reducing colon cancer mortality as well. A nonrandomized trial and indirect evidence support the use of combination FOBT and sigmoidoscopy. Indirect evidence from diagnostic accuracy studies suggests that double-contrast barium enema or virtual colonoscopy may also be effective compared with no screening. Data are insufficient to determine with confidence and precision the most effective or cost-effective strategies or the age at which screening should be stopped.

Conclusions: Colorectal cancer screening is effective in reducing mortality from colorectal cancer. Current data are insufficient to determine the most effective or cost-effective strategy for screening, although all major strategies have favorable cost-effectiveness ratios compared with no screening.

Chapter 1. Introduction

Burden of Suffering and Epidemiology

Colorectal cancer is the fourth most common form of cancer in the United States and has the second highest mortality rate, accounting for about 130,000 new cases and about 56,000 deaths in the year 2000.[1] The incidence of colorectal cancer is low until ages 45 to 50 years; it then rises throughout the remainder of a person's lifetime. Mortality from colorectal cancer begins to rise about 10 years after incidence rises. Men are slightly more likely to develop colorectal cancer than women, but the risk is high enough for both men and women potentially to benefit from screening; African-Americans are more likely to die from colorectal cancer than caucasians. Figure 1 shows the incidence and mortality of colorectal cancer by age and gender.[2] A 50-year-old person has about a 5% lifetime risk of being diagnosed with colorectal cancer and a 2.5% chance of dying from it.[3] Currently, 35% to 40% of patients diagnosed with colorectal cancer are detected when the cancer is localized; 35% to 40% have regional spread; and 20% to 25% have distant metastases.[2] Estimated 5-year survival is greater than 90% in persons with Dukes' Stage A cancers, 80% for Dukes' Stage B, 65% in persons with regional spread (Dukes' C), and 8% in those with Stage D cancers (distant metastases). The average patient dying of colorectal cancer loses 13 years of life.[1]

Polyps and Cancer – There are two types of polyps: hyperplastic and adenomatous. Hyperplastic polyps do not become cancers and require no further attention here. Some adenomatous polyps develop into cancer but most will not. The prevalence of adenomatous polyps at age 50 is 20% to 25%; this level increases to 50% by ages 75 to 80.[3] Limited data suggest that less than 1% of small adenomatous polyps (smaller than 1 cm in size) will eventually develop into cancer. Of large polyps (larger than 1 cm in size), about 10% will become malignant within 10 years and about 25% after 20 years.[4] Our current understanding of the biology of colorectal neoplasia suggests that most (more than 80%) of colorectal cancers arise from precancerous adenomatous polyps ("adenomas").

Risk Factors for Colorectal Cancer

More than 60% of colorectal cancers occur in persons at average risk. Table 1 shows the relative risk of colorectal cancer for persons with certain characteristics. Approximately 20% of colorectal cancer cases occur among patients with a family history of colorectal cancer in a first-degree relative.[5] In an analysis of 2 large cohorts involving more than 840,000 patient-years of follow-up, a family history of colorectal cancer was associated with a significant increase in risk in younger persons (1.7- to 4-fold increase between ages 40 and 60) but not with a significantly increased risk for persons older than age 60; risk was higher in persons with more than 1 affected relative.[6] Six percent of colon cancers occur among persons with uncommon hereditary syndromes (e.g., familial adenomatous polyposis [FAP] or hereditary nonpolyposis colorectal cancer [HNPCC]) that confer a high risk of colorectal cancer. Persons with longstanding ulcerative colitis are at increased risk, as are persons with a history of large adenomatous polyps or colorectal cancer.[3,7] Adenomatous polyps diagnosed in a first-degree relative before age 60 increases the risk of colorectal cancer (relative risk [RR]=1.78; 95% confidence interval [CI] 1.18 — 2.67).[8] A prior diagnosis of endometrial or ovarian cancer also conveys increased risk,

particularly for cancers occurring below age 50; a history of breast cancer increases risk only slightly, if at all.[9-11, 12,12,13,13]

The relationship between diet and colon cancer has been the subject of extensive epidemiologic research. Numerous observational studies have examined whether certain dietary elements are associated with an increased or decreased incidence of colon cancer or adenomatous polyps.[14] Diets low in fat and red meat, and high in fiber and fruits and vegetables, have been associated with lower risks of colorectal cancer, but no evidence shows that changes in diet affect the subsequent rate of new cancers. High levels of physical activity are also associated with lower rates of colorectal cancers but, again, it is unclear if this relationship is causal or if it is confounded by other factors.[15] A full examination of the observational evidence regarding the relationship between dietary functions or physical activity and colorectal cancer is beyond the scope of this paper.

Prior Task Force Recommendations

In 1996 the USPSTF recommended screening for colorectal cancer with fecal occult blood testing (FOBT), sigmoidoscopy, or both tests.[16] The USPSTF did not recommend for or against other means of screening (digital rectal examination [DRE], barium enema, colonoscopy) on the grounds that evidence was insufficient. They also recommended that FOBT be performed yearly but did not specify an interval for sigmoidoscopy.

To update the 1996 review and provide the scientific evidence for the USPSTF to make new recommendations, we undertook a systematic review of screening for colorectal cancer in average-risk adults. Related questions, such as screening of higher-risk patients, surveillance of patients with previous polyps or cancers, or diagnosis of patients with colon-related symptoms, are mentioned briefly but were not reviewed for this report.

Chapter 2. Methods

We document here the procedures that the Research Triangle Institute - University of North Carolina Evidence-based Practice Center (RTI-UNC EPC) used to develop this systematic review on screening for colorectal cancer.[17] We describe development of the analytic framework and key questions, management of the literature search and synthesis, and conduct of the external peer review process. During these steps, EPC staff collaborated with two members of the USPSTF who acted as liaisons for this topic; they are co-authors of this review. The interactions took place chiefly by electronic mail and telephone conference calls. Steps in the development of this review were presented at USPSTF meetings in December 2000 and March 2001, when EPC staff and USPSTF members were able to discuss the analytic framework, key questions, and final draft findings and conclusions.

Analytic Framework and Key Questions

The USPSTF examined the following overarching key question related to colorectal cancer screening: What are the benefits and adverse effects of screening average-risk adults over the age of 50 for colorectal cancer with office FOBT (oFOBT) and DRE, home FOBT, sigmoidoscopy, FOBT and sigmoidoscopy together, double contrast barium enema (DCBE), colonoscopy, or computed tomography (CT) colography? Each major testing strategy was examined separately, yielding seven subsidiary key questions.

To guide the review process, the authors developed the analytic framework depicted in Figure 2. The framework begins with asymptomatic adults ages 50 and older with no special risk factors for colorectal cancer. Screening of high-risk patients is addressed separately. Average-risk adults can undergo one of several strategies for screening. The screening strategies involve 1 or more tests that are repeated at some interval. Harms, including complications of the screening test, false positives, and economic costs, can arise at the screening phase. Persons screening negative are retested after some interval of time.

Persons screening positive by any method other than screening colonoscopy then undergo diagnostic colonoscopy. If the colonoscopy is negative for adenomas and cancers, screening can be suspended for at least 5 years. If the colonoscopy identifies neoplasms, they are biopsied. Adenomatous polyps usually can be removed during the initial colonoscopy. If cancer is detected, the patient receives further diagnostic studies to assess the stage of disease and then receives treatment (usually surgery, with radiotherapy or chemotherapy as adjuvant therapy in some circumstances). Harms can again arise at the time of colonoscopy or from treatment. Detection and removal of adenomas can prevent future cancers. Early detection and treatment of early-stage cancers can reduce colorectal cancer mortality.

Literature Searching and Analysis

We used the second edition of the *Guide to Clinical Preventive Services,* existing systematic reviews, focused MEDLINE literature searches from 1966 through September 2000, review of the British National Health Service Economic Evaluation database, and hand-searches of key articles to identify the literature relevant to our key question. For those questions for which we performed MEDLINE searches, 1 reviewer examined the abstracts of the articles identified in the initial search to determine relevancy. A second reviewer examined the excluded articles and

differences were resolved by consensus. Two reviewers examined the full text of the remaining articles to determine final eligibility.

We then abstracted the final set of eligible articles and created evidence tables. When systematic reviews were considered for inclusion, two investigators examined each review to assure that it followed methods similar to those used in our searches.

Peer Review Process

A draft version of this report underwent review by several content experts and stakeholders (see acknowledgements). Based on their comments and those of the USPSTF members, the report was revised.

Chapter 3. Results

Our main question concerns the evidence about the benefits and adverse effects of different colorectal cancer screening strategies for average-risk adults. The available screening tests for colorectal cancer are the DRE (with or without a single office-based FOBT), home FOBT, sigmoidoscopy, DCBE, colonoscopy, and CT colography. Each of these approaches, as well as the combination of FOBT and sigmoidoscopy, has been considered as a means of screening for colorectal cancer. Other combinations of tests have not been well evaluated and are not discussed here.

We review here the evidence about the accuracy and effectiveness of the above screening strategies for average-risk adults. When available, we focus on evidence from trials or observational studies that have measured patient outcomes, particularly changes in colorectal cancer mortality. When such data are not available, we present indirect information, such as screening test accuracy. For each modality, we also report the adverse effects or harms associated with its use and its acceptability to patients. In each case, we attempt to consider the entire screening pathway, rather than just the initial test itself.

Digital Rectal Examination and Office Fecal Occult Blood Testing

Although DRE with a single office-based FOBT is commonly performed by practitioners, the effectiveness of this approach in reducing colorectal cancer mortality has not been studied directly in a clinical trial or observational study. Evaluation of its effectiveness can be based only on indirect information, mostly regarding test accuracy.

DRE — The sensitivity of a screening DRE is low: less than 10% of colorectal cancers arise within reach of the examining finger.[3] Some of these lesions will be symptomatic and thus the sensitivity of DRE in asymptomatic adults over 50 with colorectal cancer is likely to be even lower. The specificity of a positive DRE has not been examined in average-risk outpatients.

A case-control study from Northern California Kaiser Permanente examined the effect of screening DRE on mortality from colorectal cancer.[18] The investigators identified Kaiser patients ages 45 and older who died of distal rectal cancers between 1971 and 1986 and selected matched controls from their patient membership. They examined medical records to determine if cases and controls had undergone screening DREs within a year of diagnosis and found no difference between groups after controlling for potential confounders (adjusted odds ratio, 0.96; 95% CI, 0.56 - 1.7). Checking longer periods of time before diagnosis did not change the results. Their findings did not support a relationship between DRE and risk reduction of death from distal rectal cancers, although the confidence interval was wide and did not exclude an important protective effect.

Office FOBT — The value of a single office-based FOBT obtained at the time of the DRE is also based on indirect evidence. Theoretically, oFOBT should be less sensitive than the traditional 3-sample home-performed FOBT because only 1 sample is taken. In addition, the failure to allow the degradation of vegetable peroxidases that sometimes produce false-positive results and the potential trauma from the examination itself have been proposed as reasons that the oFOBT may also be less specific (able to produce a negative result when no colorectal cancer is present) than a properly performed home FOBT.

Published studies of FOBT have shown that the yield of the 3-sample card strategy is higher than that for the first sample card alone. Yamamoto and Nakama found that the first test card

detected 58% of cancers found in a large study of FOBT in Japan.[19] The second card increased the yield to 89% and the final card to 100%. Almost half (42%) of the cancers detected would have been missed by using only the first card.

Two studies have compared retrospectively the specificity of oFOBT and home FOBT. Bini et al. examined the records for 672 patients who were referred for colonoscopy because of a positive FOBT.[19] The positive predictive values (PPV) for cancer were similar in each group (11.7% for oFOBT; 11.3% for home FOBT). Sensitivity could not be evaluated. Although the study attempted to exclude patients with abdominal signs and symptoms, the nonrandomized nature of the comparison made it difficult to determine if the 2 groups (those receiving oFOBT and those receiving home FOBT) had an equal risk for colorectal cancer. If the risks were different, then these results cannot be interpreted as demonstrating equivalent specificity.

Eisner and Lewis performed a similar study among 270 patients with positive FOBT (144 obtained on oFOBT from a DRE, 126 on home FOBT) referred for colonoscopy.[20] The 2 groups had a similar frequency of colonic abnormalities. However, patients with positive oFOBT on DRE were mostly inpatients (77%), whereas those with positive results obtained on home FOBT were not (17%). This finding suggests that the groups were not comparable, making conclusions about test specificity unreliable.

Fecal Occult Blood Testing

General Description — The home FOBT requires the patient to collect and submit 3 stool test cards (each card with 2 separate stool samples from each of 3 consecutive bowel movements). The intervals that have been studied are every 1 or 2 years. Because laboratory data have shown that certain dietary substances can cause inaccurate test results, patients are generally asked to restrict their diet for 3 days before and during sample collection. The cards are then returned for processing.

A positive home-FOBT result (1 or more test windows positive) requires a diagnostic examination with colonoscopy. If a positive FOBT is followed by a negative colonoscopy, FOB testing can be suspended for at least 5 years. A negative FOBT is repeated in 1 to 2 years, depending on the choice of test interval.

A process called rehydration, in which distilled water is added to the slides just before the test reagents are applied, is sometimes used to increase sensitivity of the FOBT. The increase in sensitivity, however, comes at the cost of decreased specificity.[21]

Accuracy — Determining the sensitivity and specificity of rehydrated or unrehydrated FOBT is methodologically difficult. Traditional definitions of sensitivity and specificity are based on evaluations of tests at a single point in time. Measuring the performance of a screening program entails multiple tests performed over time for each participant. Because studies of longitudinal screening have not performed a criterion standard examination (such as colonoscopy) after each test iteration, data on single-test sensitivity cannot be derived directly from the existing longitudinal trials, although methods exist to estimate it.[22] Studies that have measured the sensitivity and specificity of a single iteration of FOBT among truly asymptomatic subjects have found a sensitivity for an unrehydrated test to be approximately 40%; its specificity appears to be 96% to 98%. Rehydration increases sensitivity to 60% but lowers specificity to 90%.[21,23,23] Because the pretest probability for cancer is low, the majority of positive FOBT are false positives. The reported PPV for unrehydrated slides among asymptomatic persons over age 50 is 5% to 18% for any cancer and 20% to 40% for the combination of curable cancer or large

adenomas.[21] The PPV in the large, randomized Minnesota screening trial (described below) was only 2.2 %, using mostly rehydrated slides. The PPV for cancer and large polyps varied depending on how many of the 6 test windows were positive. When only 1 was positive, the PPV was 0.9%; for 4 positives, it was 1.9%; and for 6 positives, it was 4.5%. The PPVs for adenomas more than 1 cm in size were 6.0%, 7.5%, and 7.9%, respectively.[24,25]

For longitudinal programs of screening, potentially more relevant global measures of test accuracy are the proportion of cancers identified by screening (the longitudinal analogue of single-test sensitivity) and the proportion of patients requiring a criterion standard examination but not diagnosed with cancer (the longitudinal analogue of the false-positive rate or 1 minus specificity). In the annual screening arm of the 13-year Minnesota trial, which used primarily rehydrated test cards and had a high initial rate of participation (about 90%), 49% of patients who developed colorectal cancer were identified through screening; 38% of all patients had had at least 1 colonoscopy. With biennial testing, 39% of cancers were detected by screening and 28% required colonoscopy. In the European trials in the United Kingdom and Denmark, which were population based and 8 to 10 years in duration, researchers used biennial testing and had lower rates of participation (60% to 70% completed first screen), 27% of cancers were detected by screening (49% of cancers occurring in participants); only 5% of patients underwent colonoscopy.[24,26,27]

Eddy developed a model of colorectal cancer screening that projected that a patient undergoing annual unrehydrated FOBT from age 50 to age 75 has an estimated 45% probability of receiving a false-positive result.[28] Long-term data are not available to validate this estimate.

Other stool tests have been proposed to improve the accuracy of screening for fecal occult blood. Although some newer techniques, including quantitative measures of heme and genetic stool markers, hold promise, they have not been evaluated with respect to mortality reduction (as the Hemoccult™ FOBT has been).[21,29 29]

Effectiveness — The effectiveness of FOBT for reducing colorectal cancer mortality has been examined directly in 3 randomized controlled trials. All trials used the Hemoccult™ test kit. Among these 3 trials, risk of death from colorectal cancer was decreased by 15% to 33% (Table 2). The two trials with smaller reductions in mortality (15% and 18%) were conducted in Europe (the United Kingdom and Denmark), randomized patients prior to agreement to participate and thus had lower participation rates, used biennial screening, and did not perform rehydration.

The third trial, conducted in Minnesota, randomized volunteers, used annual and biennial testing, and rehydrated most test cards (83%). Cumulative mortality from colorectal cancer was 33% lower among persons randomized to undergo annual FOBT (5.9 deaths per 1,000) than among a control group that was not offered screening (8.8 deaths per 1,000). In the original report of the Minnesota trial, those assigned to biennial screening did not show a reduction in mortality; however, a recent report after 18 years of follow-up showed that a significant 21% reduction in mortality difference had emerged.[30] Another recent report from the 18-year follow-up of the Minnesota trial showed that the incidence of colorectal cancer was decreased by 20% and 17% for the annual and biennial groups, respectively, compared with controls.[25]

A fourth trial conducted in Sweden has not reported mortality results. However, previously unpublished data described in the systematic review by Towler et al. suggests that the Swedish investigators did not find a significant mortality reduction after 2 rounds of rehydrated testing (RR = 0.88; 95% CI, 0.69 - 1.12).[31]

Adverse Effects — FOB testing itself has few adverse effects, but false-positive FOBTs lead to further tests, such as colonoscopy, during which adverse effects may occur. The specific adverse effects of colonoscopy are described below. Theoretically, a previously negative FOBT could falsely reassure patients and lead to delayed response to the development of colorectal symptoms if a cancer were to develop, but this concern has not been evaluated empirically.

Acceptability — Some patients report that they find the FOBT unpleasant or difficult to perform. Nevertheless, initial rates of FOBT completion when the test is ordered by the patient's provider have been reported to be 50% to 70% and can be increased by an average of 14% with the use of a reminder system.[32,33] The rates of long-term adherence have not been well studied except in the randomized trials of screening. In those trials, about 50% of participants completed all tests in the series; 80% of initial acceptors completed the second test in the series.[32] When offered the choice of FOBT alone, sigmoidoscopy alone, or both tests together, 36% to 53% of subjects in one clinic-based study preferred FOBT alone, depending on the amount of information provided and the imposition of co-payments for sigmoidoscopy.[34]

Sigmoidoscopy

General Description — Sigmoidoscopic screening today is performed with a 60 cm flexible endoscope. The test, also referred to as flexible sigmoidoscopy or "flex sig," is generally recommended every 5 years, though no empiric data testing different intervals are available. To prepare for the test, patients are usually asked to take 2 enemas the morning of the examination. No sedation is used. If a screening examination detects cancer, large adenomatous polyps (greater than 1 cm), sessile polyps, or carcinoma *in situ*, a colonoscopy is then performed. If no polyps are found, the sigmoidoscopy is repeated in 5 years.

The question of which findings on sigmoidoscopy should trigger immediate colonoscopy is a matter of ongoing debate. Some researchers advocate performing colonoscopy when any polyp is detected; others have recommended performing colonoscopy only after detection of large, multiple, or high-risk adenomas. Recent data suggest, however, that although finding large or high-risk adenomas in the distal colon increases the chance that high-risk proximal adenomas are also present, the finding of small adenomas or hyperplastic polyps also increases that chance somewhat. The decision about when to perform colonoscopy requires a decision about what chance of missing an important proximal finding is acceptable.[35,36]

Accuracy — First-time sigmoidoscopic screening in asymptomatic persons detects about 7 cancers and 60 large or high-risk adenomas per 1,000 examinations.[37] The 60-cm instrument has an average depth of insertion of 40 to 50 cm. It will reach the proximal end of the sigmoid colon in 80% of examinations.[38] Because the sigmoidoscope can examine only the distal portion of the colon, important proximal lesions may not be identified. The actual proportion of patients who will have an important proximal lesion missed, however, will include only those patients who do not have any distal lesions that would trigger colonoscopy.

Two recent studies have examined the question of what proportion of patients with cancer or advanced adenomas will be missed with sigmoidoscopy, stratifying their results on the basis of different potential rules for which findings on sigmoidoscopy trigger full colonoscopic examinations.[35,36] Lieberman et al. conducted such a study among 3,121 patients in the Department of Veterans Affairs system.[35] They found that 80% of the 329 patients with advanced adenomas (defined as adenomas that were over 1 cm in size, multiple, or had villous features) had at least one adenoma (of any size) in the distal colon, defined as distal to the

splenic flexure. If the distal colon were defined as only the rectum and sigmoid, this figure fell to 68%. The type of distal adenoma was associated with the likelihood of an advanced proximal lesion, but the finding of no distal lesion did not rule out the possibility of a proximal lesion. Imperiale et al. conducted a similar study among 1994 adults ages 50 and older, who were taking part in a workplace screening program.[36] Overall, 104 patients had advanced neoplasms, defined as those lesions larger than 1 cm or having villous features, high-grade dysplasia, or carcinoma *in situ*. Overall, sigmoidoscopy would have detected 81 of the 104 patients with advanced lesions (78%). Assuming patients with an advanced distal finding all would under colonoscopy. Sigmoidoscopy can also produce false-positive results, by detecting either hyperplastic polyps that do not have malignant potential or adenomatous polyps that are unlikely to become malignant during the patient's lifetime. Studies of diagnostic accuracy cannot measure whether adenomas (small or large) identified and removed would have gone on to become cancers, so investigators have not typically counted them as false positives. This decision means that evaluation and comparison with other methods such as FOBT are difficult.

Effectiveness — Thiis-Evensen et al performed a small randomized trial of sigmoidoscopy screening in Norway.[39] In 1983, they randomized 799 men and women ages 50-59 drawn from a population registry to be offered screening flexible sigmoidoscopy (400 patients) or to be controls (399 patients). Intervention patients were contacted and asked to participate in screening; control patients were not contacted until the study's conclusion in 1996. All patients with polyps on sigmoidoscopy underwent immediate diagnostic colonoscopy and had surveillance examinations 2 and 6 years later. All study participants (intervention and control) were offered endoscopic testing in 1996.

Of the 400 intervention patients, 324 (81%) agreed to have sigmoidoscopy in 1983. Approximately 34 percent (34.6%) were found to have at least one polyp, (defined as any circumscribed, elevated lesion) and 1 person was found to have cancer on the initial examination. Over the 13-year course of the trial, 2 colorectal cancers were diagnosed in the intervention group and 10 in the control group (RR for colorectal cancer incidence = 0.2; 95% CI, 0.03 - 0.95). One person who was assigned to the intervention group, but who never had a screening examination, died from colorectal cancer; 3 deaths occurred in the control group (RR = 0.50; 95% CI, 0.10 - 2.72). Overall mortality was higher in the intervention group than in the control group (14% vs. 9%; RR=1.57; 95% CI, 1.03 - 2.40), mostly because of an excess of cardiovascular deaths. There was no clear relationship between the excess deaths and any complications from the procedures. The authors reported only 1 complication (water intoxication from an excessive preparation regimen) in 788 colonoscopic examinations, 432 sigmoidoscopic examinations, and 1,734 polypectomies.

These data suggest that sigmoidoscopic screening with colonoscopic follow-up for any positive finding may be effective in reducing the incidence of future colorectal cancer. They also suggest the possibility of a reduction in mortality from colorectal cancer, although the study was too small to estimate precisely the magnitude of benefit.

Two ongoing trials using flexible sigmoidoscopy can be expected to report their initial results within 5 years. One trial is examining the effect of once-in-a-lifetime sigmoidoscopy in the United Kingdom;[37] a second trial in the United States is examining sigmoidoscopy every 5 years with the assumption that patients are receiving FOBT as well.[40]

Well-designed case-control studies have provided important information on the effectiveness of sigmoidoscopy screening. Selby et al. examined data from Northern California Kaiser Permanente and found that 9% of persons who died of colorectal cancer occurring within 20 cm

of the anus had previously undergone a rigid sigmoidoscopic examination, whereas 24% of persons who did not die of a cancer within 20 cm of the anus had received the test.[41] The adjusted odds ratio of 0.41 (95% CI, 0.25-0.69) suggested that sigmoidoscopy screening reduced the risk of death by 59% for cancers within reach of the rigid sigmoidoscope.
The investigators noted that the adjusted odds ratio for patients who died of more proximal colon cancers was 0.96. This finding added support to the hypothesis that the reduced risk of death from cancers within reach of the rigid sigmoidoscope could be attributed to screening rather than to confounding factors. The risk reduction associated with sigmoidoscopy screening did not diminish during the first 9 to 10 years after the test was performed.[41] Although the Selby et al. study mostly used rigid sigmoidoscopes, in another case-control study supporting the effectiveness of sigmoidoscopy, 75% of the examinations were performed with a flexible instrument.[42]

Adverse Effects — Estimates of bowel perforations from sigmoidoscopy have generally been in the range of 1 to 2 per 10,000 examinations or lower, particularly since the introduction of the flexible sigmoidoscope.[43] Atkin et al. recently reported initial results from their sigmoidoscopy screening trial.[37] Experienced endoscopists performed sigmoidoscopy in 1,235 asymptomatic adults ages 55 to 64 years; 288 patients had polyps removed during the examination. Adverse effects, including pain, anxiety, or any degree of bleeding, were assessed by a written questionnaire immediately after the test and by a postal questionnaire 3 months later. Of all subjects, 3.2% (40/1,235) reported bleeding (16/288 or 5.5% after polypectomy; 24/947 or 2.5% of only diagnostic studies); 1 patient required admission; none required a transfusion. Of all subjects, 14% reported moderate pain and 0.4% reported severe pain. More than 25% of patients reported gas or flatus. No perforations were reported, but 1 patient died from peritonitis after a complicated open surgical procedure to remove a severely dysplastic adenoma. A recent study of endoscopic complications from the Mayo Clinic in Arizona identified 2 perforations during sigmoidoscopy out of 49,501 procedures.[44]

Acceptability — Studies examining the acceptability of sigmoidoscopy to patients have reached mixed results, depending on the setting and whether the evaluation was prospective or retrospective. Studies conducted in primary care settings have found rates of adherence of 25% to 50% for the initial test, but data are insufficient to predict the proportion of patients who will continue to complete subsequent examinations in a program of screening. [32] When given information about screening options and offered the choice of FOBT alone, sigmoidoscopy alone, or both tests together, most patients in an academic internal medicine clinic preferred both tests or FOBT alone; only 8% to 13% preferred sigmoidoscopy alone, suggesting that patients willing to undergo sigmoidoscopy usually are also interested in FOBT. [34]
Verne et al., compared the acceptability of FOBT alone, flexible sigmoidoscopy alone, or the combination of the 2 tests in a randomized controlled trial.[45] They identified 3,933 patients ages 50 to 75 years from the registry of a general practice in Great Britain. One of the investigators, a practitioner in the clinic, excluded 5% of the patients as ineligible because they had died, moved away, been diagnosed previously with colorectal cancer, or had been recently screened. Potentially eligible subjects were randomized to receive by mail an invitation to FOBT, sigmoidoscopy, or both tests. Those invited to do FOBT received the Hemoccult™ cards in the mail; those invited to do sigmoidoscopy were sent an appointment and the preparatory material. Those randomized to be offered both tests were asked to do the FOBT first.

Subjects assigned to sigmoidoscopy alone were more likely to complete their test than subjects assigned to FOBT (47% vs. 32%). Subjects offered both tests completed them both

30% of the time. More subjects in the combined group completed sigmoidoscopy than FOBT (38% vs. 32%).[45,46]

FOBT and Sigmoidoscopy

General Description — The strategy of combining FOBT every year and sigmoidoscopy every 5 years involves many of the same issues that are described for each test individually. If either test is positive, colonoscopy is performed. Therefore, in a year in which both tests are due, it is prudent to perform FOBT first, so that if it is positive, colonoscopy can be performed instead of sigmoidoscopy.

Effectiveness — Currently no randomized trials with colorectal cancer mortality as an endpoint compare the performance of FOBT alone or sigmoidoscopy alone against a strategy of performing both tests.

Winawer et al. conducted a nonrandomized study of more than 12,000 first-time attendees at a preventive health clinic in New York.[47] Participants were assigned to 1 of 2 groups. The control group received a rigid sigmoidoscopy examination at the first visit and was invited to return for annual re-checks. Intervention patients received the rigid examination and were also asked to complete Hemoccult™ FOBT cards. Patients with adenomas more than 3 mm on sigmoidoscopy or a positive FOBT underwent full colonic examination with barium enema and colonoscopy. Few subjects continued to participate after the first examination (20% had FOBT at year 2 and 15% at year 3). Incidence of colorectal cancer and mortality were assessed over a 9-year period; follow-up data were available for 97% of subjects.

Demographic and clinical data suggest that the groups were comparable, despite the absence of randomization. More colorectal cancers were detected on initial examination among intervention patients than control patients (4.5 vs. 2.5 per 1,000 participants). Incidence rates (cancers detected after the initial examination) were similar between groups (0.9 per 1,000 person-years in each group). Colorectal cancer mortality was 0.36 per 1,000 patient years in the intervention group and 0.63 per 1,000 patient-years among controls ($p = 0.11$).

Thus, adding FOBT to rigid sigmoidoscopy appears to increase the yield of initial screening and may reduce mortality. Because rigid sigmoidoscopy is no longer used for screening, the generalizability of these results to the use of FOBT plus flexible sigmoidoscopy is unclear. It is also unclear if the incremental yield of combined screening will change after additional rounds of testing.

Accuracy — Recent randomized trials from Europe have examined the additional diagnostic yield from performing sigmoidoscopy in addition to FOBT at one point in time for patients who were not part of an ongoing screening program.

Berry et al. randomized patients in the UK to receive an invitation for FOBT alone or an invitation for FOBT followed by an invitation for flexible sigmoidoscopy.[48] They examined the rate of acceptance of the tests and the yield for "significant neoplasia" (cancers or large polyps). Subjects had a mean age of 61 and slightly more than half were women.

The investigators found that about 50% of subjects in each group accepted and completed FOBT. Of those accepting FOBT in the combined testing arm, 20% also accepted sigmoidoscopy. In the FOBT only group, 6 significant lesions were detected (4 large polyps, 2 cancers) a yield of 2/1000 patients randomized. In the combined group, 7 patients had significant lesions based on FOBT (6 had large polyps, 1 had cancer). The addition of sigmoidoscopy identified 20 additional patients with large polyps and 2 additional patients with cancers, a yield of 8.9/1000

patients randomized. Therefore, the additional yield of important lesions was 6.9 per 1,000 patients randomized for combined testing, despite the low uptake of sigmoidoscopy. Among patients completing their tests, the yield for the combined strategy was 44.2 per 1,000 compared with 4.2 per 1,000 in the FOBT-only group.

Rasmussen et al. performed a similar trial in Denmark.[49] They randomized almost 11,000 residents of Funen, Denmark, to be offered either a single FOBT or a FOBT and a flexible sigmoidoscopy. Among those randomized to FOBT alone, 56% completed the test. In the FOBT-plus-sigmoidoscopy group, 40% completed both tests, 2% completed one of the assigned tests but not the other, and 58% did not complete any test. In the FOBT-only group, 73 subjects had a positive test (2.4% positive rate); 4 patients were found to have cancer, 14 had large polyps, 7 had small polyps, and 48 were false positives. In the combined testing group, 488 of 2,222 subjects (22%) had a positive test, defined as a positive FOBT or the finding of any polyp larger than 3 mm or cancer on sigmoidoscopy. Of the 488 positives, 12 had cancer, 72 had large polyps, 181 had small polyps, and 223 were false positives. Many of the neoplasms were detected only by sigmoidoscopy (5 of 12 cancers, 60 of 72 large polyps, 175 of 181 small polyps); no cancers and only 1 large polyp were detected by a positive FOBT when the sigmoidoscopy was negative.

The investigators also used cancer registry data to examine the effect of screening on colorectal cancer incidence 2 to 5 years after the tests were performed. The total numbers of cancers diagnosed in each group were equal, but more cancers in the FOBT-only group were detected clinically rather than by screening (18 of 22 for FOBT only versus 8 of 20 for those assigned to both tests, $p = 0.01$). Cancers detected clinically were more advanced in stage than those detected by screening, but the trial was not powered sufficiently to examine the effect on mortality.

Verne et al. used data from a general practice in Great Britain to examine the yield of 1 round of screening for patients assigned to FOBT alone, flexible sigmoidoscopy alone, or both tests together.[45] All persons with a positive FOBT underwent colonoscopy. Persons with large polyps on sigmoidoscopy underwent colonoscopy as well. Persons with polyps less than 5 mm detected in the rectum on sigmoidoscopy were biopsied: those with hyperplastic polyps did not undergo colonoscopy, but those with adenomas did.

Seven patients had a positive FOBT: 1 had a Duke's Stage C cancer, 1 had a large (2 cm) adenoma; 1 a single 2 mm adenoma; and 1 had 2 small adenomas. The 3 other patients had no findings. What proportion also had positive sigmoidoscopies was not clear.

Among the 401 subjects who completed both tests, 31 had adenomas on sigmoidoscopy (all less than 1 cm) and 1 had a Stage A cancer. This cancer and 30 of the 31 polyps were negative on FOBT. These findings suggest that adding sigmoidoscopy significantly increases the yield over FOBT alone. The data are insufficient to determine the additional yield of adding FOBT to sigmoidsocopy alone.[45]

Thus, the combination of FOBT and sigmoidoscopy apparently has a greater yield for significant neoplasia (cancers and large polyps) than does FOBT alone. According to data from the 3 European trials, adding FOBT does not seem to increase the yield obtained with sigmoidoscopy alone, after one round of testing.[45,47,49-51] Winawer et al., however, did find an increased yield from adding FOBT to rigid sigmoidoscopy and also showed a mortality reduction that was of borderline statistical significance; the data are limited because the compliance was very low for subsequent rounds of testing.[47] The incremental yield of combined testing after the first round may be different, but its impact has not been fully evaluated.

Adverse Effects — The adverse effects for the combined strategy of FOBT and sigmoidoscopy are the sum of the adverse effects of each test alone.

Acceptability — The acceptability of doing both FOBT and flexible sigmoidoscopy is affected by the downsides and effort of both tests. Nevertheless, data from an academic internal medicine clinic suggest that more than one-third of informed patients prefer to have both tests rather than either one alone.[34] Verne et al. found that adherence to combined testing was lower than that for sigmoidoscopy alone or FOBT alone (signoidoscopy alone 47%, FOBT alone 32%, both tests 30%).[45] The acceptability of both tests compared with colonoscopy or barium enema has not been evaluated.

Double Contrast Barium Enema

General Description — The double contrast barium enema (DCBE) is a radiologic test in which barium and air are instilled in the colon and x-rays are made in various positions. Patients usually prepare for the test with a laxative the night before the examination, a clear liquid diet, and 1 or 2 enemas the morning of the test. The examination itself takes 20 to 40 minutes. No sedation is used. If the test is positive, a colonoscopy is performed; if it is negative, it is repeated in 5 years.

Accuracy — We identified 12 studies from our literature search that met our criteria for inclusion in the analysis of the accuracy of DCBE in the diagnosis of colorectal cancer or adenomatous polyps.[50-61]

Many of the studies of DCBE accuracy were performed in patients with known disease; some of these patients had originally been diagnosed because of a positive DCBE and thus may overestimate accuracy. Others have looked retrospectively at patients with known disease to determine whether a barium enema had been performed within some period before diagnosis. In these studies, the sensitivity can be distorted depending on the time interval before diagnosis that is examined for "false negative" DCBE examinations. In addition, these patients (who had DCBE for some indication) may differ systematically from screening patients.

In general, these studies have found sensitivity levels of 80% to 90% for cancer, but these data cannot be extrapolated to screening with confidence. Bloomfield, in his prospective study from Australia, examined the sensitivity and specificity of DCBE for colorectal cancer and polyps;[54] he found that sensitivity was 86% and specificity was greater than 95% when detection of either a polyp or cancer was considered to be a positive finding.

The ideal study for measuring the accuracy of DCBE would examine test performance among a sample of asymptomatic patients undergoing screening. Each patient would have a DCBE examination, followed by a colonoscopy performed by an examiner masked to the result of the barium enema. In the event that lesions identified on DCBE were not seen on colonoscopy, a repeat unmasked colonoscopic examination would be performed immediately after the first colonoscopy to determine if a lesion was truly present. Results would be reported separately for large adenomatous polyps and cancer. Such a study has not been performed to date; sensitivity and yield will likely be higher on the first examination than they will on subsequent examinations of patients who initially test negative.

The National Polyp Study is a randomized trial of different intervals of surveillance (examinations at 1 and 3 years vs 3 years only) after polypectomy. In this study, Winawer et al. measured the accuracy of DCBE as compared with colonoscopy, using the technique of comparing DCBE with masked and then unmasked colonoscopy.[62] A total of 580 patients (74%

men, 61% over age 60) who had been diagnosed with adenomatous polyps had 1 or more paired examinations 1, 3, or 6 years after initial detection and removal of polyps. The paired examination consisted first of a colonoscopy performed by an endoscopist masked to the DCBE result; after the first test, any lesions identified on DCBE that had not been detected on the first colonoscopy were then looked for again on a second examination. The sensitivity of DCBE (compared to colonoscopy) for polyps less than 0.5 cm was 32% (95% CI, 25%-39%); for polyps 0.6 to 1 cm, it was 53% (95% CI, 40% -66%); for polyps larger than 1 cm, including 2 cancers, it was 48% (95% CI, 24%-67%). Of 470 examinations in which no polyps were identified on colonoscopy, barium enema was positive in 83 (specificity 85%).

The Winawer et al. study examined patients who recently had had colonoscopy and removal of all polyps. Their results, therefore, may have limited generalizability for screening, because screening is a situation in which most subjects will not have had a recent colonoscopic examination and polypectomy and hence may be more likely to have large polyps or cancers. However, the low sensitivity for large polyps found in this study is of concern and may limit the effectiveness of screening with DCBE.

Effectiveness — No trial has examined the ability of screening barium enema to reduce the incidence or mortality from colorectal cancer.

Adverse Effects — The estimated risk of perforation during barium enema is low. In the study from Kewenter and Brevinge, no perforations or other complications occurred among the 1,987 screening patients undergoing barium enema as part of their screening work-up.[63] Blakeborough et al. surveyed UK radiologists about the complications of barium enema during a 3-year period from 1992 through 1994.[64] All examinations were included, whether they were performed for patients who were acutely ill or not. Important complications of any type occurred in 1 in 10,000 examinations. Perforation occurred in 1 of 25,000 examinations; death occurred in 1 in 55,000 examinations, although whether such deaths resulted from the procedure is not clear.

Acceptability — Patients' acceptance of barium enema screening has not been evaluated. Studies examining the relative discomfort of barium enema and colonoscopy have produced inconsistent results. [65,66]

Colonoscopy

General Description — Colonoscopy has not been widely used as a screening test, although several centers have been testing its feasibility and accuracy.[35] No testing interval has been examined empirically, though testing every 10 years is the most commonly considered strategy. Some experts have advocated a once-in-a-lifetime examination between 55 and 65 years of age.[13]

The bowel cleansing preparation can be difficult. It may require that patients drink several liters of nonabsorbable laxative the night before the test or use a powerful laxative. The test itself is performed with conscious sedation and lasts 20 to 40 minutes. Patients need to have someone accompany them to the examination and drive them home. They are unable to return to work the same day, and some may miss a second day of work.[67]

Colonoscopy allows the biopsy and removal of polyps at the time of the screening examination itself. If cancer is detected, further assessment and treatment can be pursued. If the test is negative, it is repeated at 10 years.

Accuracy — The accuracy of colonoscopic screening is difficult to evaluate because colonoscopy is commonly used as the criterion standard exam, making the calculation of

sensitivity difficult. One method of evaluating sensitivity, tandem colonoscopic examinations, has found that the sensitivity is 90% for large adenomas and 75% for small adenomas (less than 1 cm); sensitivity for cancer is likely to be greater than 90%.[68]

The recent identification of flat lesions that can be missed on regular colonoscopy suggests that some histologic variants do not pass through the same process of detectability as is proposed in the typical adenoma-carcinoma sequence.[69] If flat lesions account for 10% of all adenomas, sensitivity of all endoscopic screening may be lower than previously thought.

The specificity of colonoscopy with biopsy is generally reported to be 99% or 100%, but this assumes that all adenomas that are detected represent "true positives." For all forms of screening, most adenomas that are detected, especially small adenomas, will never develop into cancer. If detection of an adenoma that will not become cancer is considered a false positive that subjects a patient to risk without benefit (see complications below), then the actual "specificity" is much lower.

Effectiveness — The ability of colonoscopy to prevent colorectal cancer cases or mortality has not been measured in a screening trial. The National Polyp Study estimated that 76% to 90% of cancers could be prevented by regular colonoscopic surveillance examinations, based on comparison with historic controls.[62] However, these results should be interpreted with caution, because the comparison groups were not from the same underlying population, which could introduce bias. In addition, the participants in the trial all had had polyps detected and removed, which limits their generalizability to the average screening population.

Muller and Sonnenberg, in a case-control study at VA hospitals, found that patients diagnosed with colorectal cancer were less likely to have had previous endoscopic procedures: the odds ratio for colon cancer was 0.51 (95% CI, 0.44-0.58) and for rectal cancer, 0.55 (95% CI, 0.47-0.64).[70] When colonoscopy was considered alone, the odds ratios were 0.47 (95% CI, 0.37-0.58) and 0.61 (95% CI, 0.48-0.77), respectively.

The reduction in colorectal cancer incidence and mortality from prevention and early detection with screening colonoscopy every 10 years has been estimated in recent colorectal cancer screening models to be 58% (incidence reduction) and 61% (mortality reduction).[71]

Adverse Effects and Costs — Colonoscopy, which requires sedation and skilled support personnel, is more expensive than other screening tests and has a higher risk of procedural complications, particularly when polypectomy is performed. The use of conscious sedation adds the risk of complications attributable to the anesthetic.

We conducted a systematic review of studies examining the principal complications of colonoscopy. We focused on hemorrhage and perforation but noted the less frequent complications of death, infections, sedation-related events, and chemical colitis as well. We identified 19 articles that examined complications of colonoscopy (see Table 3).[35,36,43,44,67,72-85]

Two recent studies examined the incidence of complications from colonoscopy performed in screening populations.[35,36] One study was conducted among patients in Veterans' Affairs medical centers and another among employees of a large corporation using experienced, highly skilled endoscopists. In the VA study by Lieberman et al, 10 of 3121 patients (0.3%) had major complications during or immediately following the procedure, including 6 who had bleeding requiring hospitalization and 1 each with a stroke, myocardial infarction, Fournier's gangrene, and thrombophlebitis.[35] Three other patients died within one month, though the authors did not believe the deaths to be related to the procedure. In the study by Imperiale et al, 1994 patients ages 50 and older underwent colonoscopy.[36] One (0.05%) had a perforation that did not require

surgery and 3 (0.15%) had bleeding that required emergency room visits but not admission or surgery. There were no deaths.

Apart from these 2 screening studies, most of the studies we identified were retrospective reviews of endoscopy records from US university hospitals. Publication dates ranged from 1982 to 2000 for reviews of data between 1972 and 1997. Two studies used prospective data questionnaires to assess complications more fully.[67,73]

Fewer than half of the studies distinguished between diagnostic and therapeutic procedures (those in which a polypectomy was performed). The proportion of patients undergoing screening, follow-up, or surveillance examinations versus procedures for symptomatic processes varied among the studies included; moreover, this information was not reported for several studies, making extrapolation to screening difficult.

The rates of perforation for diagnostic procedures were low, ranging from 0.029% to 0.61%. Most studies did not give the rate of post-colonoscopy bleeding following diagnostic procedures. In 1 prospective study of 250 patients undergoing diagnostic procedures no bleeding events and no perforations had occurred after 24 hour follow-up.[67] The complication rates for therapeutic procedures were higher: 0.07% to 0.72% for perforations and 0.2% to 2.67% for bleeding. Deaths occurred infrequently and were more likely to occur in symptomatic patients with acute problems or those with comorbid conditions. The death rates reported ranged from 0.0037% to 0.06%. The mortality rate for screening may be on the lower end of this range; 1 cost-effectiveness analysis estimated it as 1 per 20,000 patients.[23] Other clinically relevant complications were identified too infrequently and measured too inconsistently to estimate accurately their true incidence.

The limited number of screening studies and reliance upon information extracted from the written record or databases in the majority of other studies limit the quality of the data and their ability to accurately inform estimates of possible adverse effects from colonoscopy screening. Publication bias may also affect the accuracy of our estimates, because centers with better rates of complications may be more likely to publish their data. In addition, reports that present only an overall complication rate that mixes diagnostic and therapeutic procedures are less helpful, because the single (combined) rate probably overstates the complication rate for diagnostic procedures and underestimates it for therapeutic procedures.

Acceptability — One study has examined informed patient preferences for colonoscopy compared with other methods of screening in a population of patients that had considerable previous screening experience. The investigators found that a plurality (38%) preferred colonoscopy.[86]

Computed Tomography Colography

General Description — CT colography, also known as "virtual colonoscopy," has recently begun to be considered as a means of screening for colorectal cancer. The examination currently requires a preparation similar to colonoscopy, followed by installation of air through a rectal tube. CT scan images are then made of the colon, and a computer reconstructs them into virtual images of the colonic lumen. The test can be performed in 10 to 15 minutes. If the test is positive, the patient will need to undergo colonoscopy. If negative, they will presumably be rescreened after some interval.

Effectiveness — No studies have evaluated the effectiveness of CT colography in reducing morbidity or mortality from colorectal cancer.

Accuracy — Several studies conducted in research settings among highly skilled radiologists have evaluated the accuracy of CT colography compared with that of colonoscopy.[87,88] Initially reported sensitivity and specificity values for cancers and large polyps were in the range of 85% to 90%, but recent reports have suggested lower levels of accuracy for less experienced examiners. Small and flat polyps are less well visualized on CT colography than are cancers and large polyps**.**

Adverse Effects – The data are currently insufficient to measure the frequency of complications with CT colography**.**

Acceptability – The acceptability and feasibility of CT colography have not been examined.

When to Start or Stop Colorectal Cancer Screening

Information on the optimal age to begin or end screening and the frequency with which it should be performed is limited. The age groups in which screening has been shown to decrease mortality are ages 50 to 80 years for FOBT and age 45 and older for sigmoidoscopy.[31,41] Theoretically, the potential yield from screening should increase beyond age 50 because the incidence of colorectal cancer after this age doubles every 7 years.[1] Eddy's cost-effectiveness model suggests that beginning screening at age 40 rather than at age 50 offers less than a 1-day average improvement in life expectancy.[28]

We found no direct evidence to allow determination of the proper age for discontinuing screening. The randomized trials of screening suggest, however, that several years of life expectancy may be required to realize the benefits of screening. The optimal interval for screening is less certain for sigmoidoscopy than for FOBT, for which there is good evidence of benefit from annual and biennial screening, although annual screening appears to be more effective.

Cost and Cost-effectiveness

Several analyses have examined the cost-effectiveness of colorectal cancer screening. Our systematic review of such analyses (to be reported in a separate paper[89]) included studies of the cost-effectiveness of individual screening modalities compared with no screening and those that compared different modes of screening.

We identified 6 high-quality cost-effectiveness analyses. For 5 studies, we used the most recent complete publication.[23,28,71,89-91] [Vijan et al., personal communication] In general, the studies focused on the impact of screening on a cohort of adults ages 50 and older who had been screened at regular intervals from ages 50 to 85 or death. Each analysis considered direct costs; none considered indirect costs such as the cost of the time required to perform screening or treatment. Most used fee schedules of Medicare or other payers to estimate costs. Results were presented as average or incremental cost in dollars per life-year saved. None attempted to quality-adjust the value of the life-years.

Our main analyses (Table 4) show average cost-effectiveness ratio values (costs per life-year saved) for each of the major strategies standardized to year 2000 dollars. Nearly all show cost-effectiveness ratios less than $30,*000* per life-year saved, supporting the finding that, compared with no screening, any reasonable strategy appears to be cost-effective using common US thresholds.

Five teams examined the incremental cost-effectiveness of different strategies.[Vijan et al., personal communication][23,71,90,91] Their conclusions about which test(s) were most effective and least costly varied between analyses and within analyses, depending on assumptions about the biologic behavior of colorectal cancer, adherence, and costs of colonoscopy (Table 5). Of the studies considering each major strategy, some found annual FOBT plus sigmoidoscopy every 5 years to have the best performance; others favored colonoscopy every 10 years. The Sonnenberg et al. analysis favored colonoscopy as well, but it did not evaluate the strategy of FOBT plus sigmoidoscopy.[91]

Screening Patients at Higher than Average Risk of Colorectal Cancer

As noted in the introduction, patients at increased risk of colorectal cancer account for about 30% to 35% of colorectal cancer cases. Considering screening patients at highest risk, such as those with rare hereditary syndromes and inflammatory bowel disease including ulcerative colitis, was beyond the scope of this review; such patients may require special care including genetic counseling. Patients with a family history of colorectal cancer are commonly encountered in primary care. They can be identified by systematic elicitation of family histories as a routine part of preventive care. Little direct evidence, however, guides the initiation, frequency, and intensity of screening for these patients. Guidelines based on expert opinion and information about the natural history of the disease have recommended beginning screening 10 years before the age at which the family member had been diagnosed.[3,8]

Chapter 4. Discussion

Overall Findings of Effectiveness and Cost-Effectiveness

Our systematic review supports the effectiveness of screening as a means of reducing colorectal cancer mortality. Table 6 summarizes the strength of evidence supporting each of the different means of screening for colorectal cancer. For FOBT, 3 high-quality randomized trials have shown disease-specific mortality reductions of 15% to 33% over 8 to 13 years. High-quality case-control studies have shown that sigmoidoscopy and possibly colonoscopy are associated with decreased mortality within the reach of the scope. The combined strategy of FOBT and sigmoidoscopy is supported by 1 nonrandomized trial showing reduction in mortality with the addition of FOBT to rigid sigmoidoscopy [47] and by indirect evidence showing increased yield with both tests compared with FOBT alone.

Although barium enema or virtual colonoscopy have not been studied as extensively as other modalities for screening, some indirect evidence suggests that they may also be effective but further data are required in screening populations. Multiple cost-effectiveness analyses have combined these indirect data and estimated that screening by any of the commonly considered strategies appears to prevent morbidity and mortality with cost-effectiveness ratios that compare favorably with other acceptable preventive strategies, such as mammography in women over age 50.

Although colorectal cancer screening is supported by strong direct and indirect evidence, current data are insufficient to define which strategy is most effective or cost-effective. In the face of good general evidence supporting screening but uncertainty about the most effective method for doing so, providers and patients may benefit from discussing the pros and cons of the different methods and incorporating patients' preferences in the decision about how to screen. Future developments with respect to new screening modalities, better chemoprophylactic agents, and improved understanding of the effects of diet and exercise on disease incidence may change the available options for reducing disease burden in average-risk patients.

Future Research Needs

Several areas of colorectal cancer screening and prevention warrant additional research. First, there is a critical need to learn more about adherence to screening among informed patients. Second, we need better data on the real-world complication rates of colonoscopic screening and polypectomy, including whether complications become more or less likely as volume increases. The accuracy of barium enema, virtual colonoscopy, and genetic stool tests (or other novel noninvasive tests) should be evaluated in screening populations. Some have called for a randomized trial of colonoscopy to determine its actual effectiveness. The cost of such a trial, particularly if colonoscopy were to be compared to other screening modalities rather than to no screening, would be quite high; and many years of follow-up would be required for differences to emerge. Additional data from randomized trials are also needed to help improve understanding of the effectiveness of chemopreventive agents such as nonsteroidal anti-inflammatory drugs, calcium, or estrogen. Behavioral factors, including physical activity, dietary fat, dietary fiber, and fruit and vegetable consumption, appear to be related to colorectal

cancer incidence; further research is needed to determine better if these relationships are causal or are the result of uncontrolled confounding.

Despite its apparent effectiveness, colorectal cancer screening is currently underutilized by age-eligible adults. The multiple reasons for low utilization include patient-, provider-, and system-specific barriers.[32] Effective colon cancer screening requires an ongoing effort. Screening with FOBT, for example, requires offering testing to 1,000 people for 10 years to save 1 life. Although this level of effort may seem inefficient or low yield, the potential benefit is large and the costs per person are small, thus, the cost-effectiveness ratio is very favorable compared with other preventive measures. Several strategies have shown effectiveness in raising screening rates, at least in some settings over the short term. These include reminder systems, patient decision aids, and mass screening efforts through employers or other organizations. Further research is needed to determine whether such systems can maintain their effect over time.

Table 1. Relative Risk of Colorectal Cancer

Risk Factors	Relative Risk (95% CI)
Family history of colorectal cancer in a first-degree relative before age 60[3]	1.7 - 4.0*
Family history of adenomatous polyps in a first-degree relative before age 60[8]	1.8 (1.2, 2.7)
Personal history of breast cancer[9]	1.1 (1.0, 1.2)
Personal history of endometrial cancer [12,13]	
Diagnosis before age 50	3.4 (2.7, 4.2)†
Diagnosis age 50-64	0.93 (1.2, 1.8)
Personal history of ovarian cancer[12,13]	
Diagnosis before age 50	3.7 (2.7, 4.8)
Diagnosis age 50-64	1.5 (1.2, 1.8)

* For patients age 40-60; older patients appear to have lower risk.

† 95% confidence interval CCI.

Table 2. Trials of Fecal Occult Blood Test

Trial Characteristics	Minn*		UK†	Denmark‡
Frequency of testing	**Annual**	**Biennial**	**Biennial**	**Biennial**
Duration of follow-up years	18	18	8	10
Hydration of slides	Yes	Yes	No	No
Requiring colonoscopy, %	38%	28%	5%	5%
Mortality reduction, %	33%	21%	15%	18%

* Minn = Minnesota; Source = Mandel et al., 1999.[30]

† UK = United Kingdom; Source = Hardcastle et al., 1996.[26]

‡ Source = Kronborg et al., 1996.[27]

Table 3. Complications of Colonoscopy

Study	Study Design (inclusive years)	Setting	Total Procedures	Perforation Rate (All)	Bleeding Rate (All)	Total Therapeutic Procedures	Perforation Rate-Therapeutic	Bleeding Rate-Therapeutic	Mortality Rate
Newcomer et al., 1999[67]	Prospective enrollment phone survey 1 week after procedure	Community based multispecialty clinic	250	NR*	NR	0	0	0	0.0000%
Eckardt et al., 1999 [72]	Prospective evaluation of complications (1995-1997)	Referral center	2500	0.08%	0.24%	429	0.23%	1.40%	0.0000%
Zubarik et al., 1999[73]	Prospective	Referral center	1196	NR	2.10%	NR	0	NR	0.0000%
Wexner et al., 1998[74]	Retrospective review	Two centers	2069	0.15%	0.10%	353	0.85%	0.57%	0.0000%
Farley et al., 1997[75]	Retrospective review (1980-1995)	Referral center	57,028	0.08%	NR	NR	NR	NR	NR
Foliente et al. 1996[76]	Retrospective review (1987-1993)	Referral center	6684	0.22%	NR	NR	NR	NR	0.0500%

Table 3. Complications of Colonoscopy (continued)

Study	Study Design (inclusive years)	Setting	Total Procedures	Perforation Rate (All)	Bleeding Rate (All)	Total Therapeutic Procedures	Perforation Rate-Therapeutic	Bleeding Rate-Therapeutic	Mortality Rate
Gibbs et al.,1996 [77]	Retrospective review of post-procedural admissions for hemorrhage (1989-1993)	Referral center	12058	NR	0.11%	NR	NR	NR	NR
Ure et al., 1995[78]	Retrospective review (early 1990s)	NR	656	0	0.61%	195	0	2.10%	0.0000%
Lo and Beaton, 1994[79]	Retrospective review (1986-1992)	Referral center	26,708	0.05%	NR	9519	0.07%	NR	0.0037%
Rosen et al., 1993[80]	Retrospective review of post-procedural admissions for hemorrhage (1987-1991)	Community based hospital	NR	NR	NR	4721	NR	0.42%	NR
DiPrima et al., 1988[81]	Prospective review + 10 day post-procedural f/u	Referral center	302	0.66%	1.66%	138	0.72%	3.60%	0.0000%

Table 3. Complications of Colonoscopy (continued)

Study	Study Design (inclusive years)	Setting	Total Procedures	Perforation Rate (All)	Bleeding Rate (All)	Total Therapeutic Procedures	Perforation Rate-Therapeutic	Bleeding Rate-Therapeutic	Mortality Rate
Nivatvongs, 1988[82]	Retrospective review of all polypectomies (1972-1986)	Referral center	1190	NR	NR	1190	0.59%	0.84%	NR
Brynitz et al., 1986[83]	Retrospective review (1975-1984)	NR	1748	0.63%	0	NR	0.7% (0.2-1.8%)	NR	0.0600%
Webb et al., 1985[84]	Retrospective review (1975-1982)	Referral center	591 (1000 polypectomies)	0	0.80%	1000	0	0.80%	0.0000%
Macrae et al., 1983[85]	Retrospective review (1971-1980)	Referral center	5000	0.12%	0.96%	1795	0.11%	2.67%	0.0600%
Nelson et al., 1982[43]	Retrospective review (1972-1980)	Urban county hospital	1207	0.24%	NR	NR	NR	NR	0.0000%

*NR= Not reported

Table 4. Average Cost-Effectiveness Ratios for Selected Screening Strategies for Colorectal Cancer*

Screening Strategy†	Study and Costs per Life-Year Saved					
	Eddy, 1990[28]	Wagner et al., 1996[23]	Frazier et al., 2000[71]	Khandker et al., 2000[90]	Sonnenberg et al., 2000[91]	Vijan et al.,‡
FOBT q1	**13,432**	16,075	13,656	17,805	**10,463**	**5,691**
FS q5	NS§	**14,141**	**12,804**	**15,630**	39,359	19,068
FOBT + FS	30,775	16,144	18,693	22,518	NS	17,942
DCBE q5	19,563	15,974	25,624	21,712	NS	NS
COL q10	NS	26,243	22,012	21,889	11,840	9,038

* Costs per life-year saved converted to year 2000 dollars. Bold typeface indicates best average cost-effectiveness ratio.

† FOBT = fecal occult blood test; FS = flexible sigmoidoscopy; DCBE = double contrast barium enema; COL = colonoscopy; q1 = every year; q5 = every 5 years; q10 = every 10 years.

‡ Vijan et al., is personal communication of unpublished data.

§ NS = Not studied

Table 5. Preferred Strategy at Different Cost-Effectiveness Levels for Each of the Cost-Effectiveness Analyses

	Preferred Strategy If Willing to Pay:			
Studies	**< $20,000 / LYS***	**$20-30,000 / LYS***	**$30-50,000 / LYS***	**$50-100,000 / LYS***
Wagner et al., 1996[23]	DCBE q5	DCBE q5	FOBT q1 + FS q5	FOBT q1 + FS q5
Wagner, et al., 1996[23].†	COL q10	FOBT q1 + FS q5	FOBT q1 + FS q5	FOBT q1 + FS q5
Frazier et al., 2000[71]	FOBT q1 + FS q5	FOBT q1 + FS q5	FOBT q1 + FS q5	FOBT q1 + FS q5
Khandker et al., 2000.[90]	FS q5	FOBT q1	COL q10	COL q10
Sonnenberg et al., 2000[91]	COL q10	COL q10	COL q10	COL q10
Vijan et al.‡	COL 55/65	COL 55/65	COL 55/65	COL 55/65

* LYS indicates life years saved; FOBT = fecal occult blood test; FS = flexible sigmoidoscopy; DCBE = double contrast barium enema; COL = colonoscopy; q1 = every year; q5 = every 5 years; q10 = every 10 years.

† Assumes a 50% sensitivity with barium enema.

‡ Vijan et al., is personal communication of unpublished data; 55/65 indicates colonoscopy performed at age 55 and 65 only.

Table 6. Strength of Evidence about Screening Strategies

Test	Direct?* Evidence	Evidence Level	Internal Validity	External Validity
Fecal occult blood testing	Y	I	G	G
Sigmoidoscopy	Y	II	G	F
Fecal occult blood testing and sigmoidoscopy combined	+/-	II	F	F
Double contrast barium enema	N	III	F	F
Colonoscopy	+/-	II	F	F

*+/- indicates not sure

REFERENCES

1. Ries LA, Wingo PA, Miller DS, et al. The annual report to the nation on the status of cancer, 1973-1997, with a special section on colorectal cancer. *Cancer.* 2000;88:2398-2424.

2. SEER Cancer Statistics Review 1973-1997. Accessed January 15, 2001. National Cancer Institute Web Page. Available at: http://seer.cancer.gov/Publications.

3. Winawer SJ, Fletcher RH, Miller L, et al. Colorectal cancer screening: clinical guidelines and rationale. *Gastroenterology.* 1997;112(2):594-642.

4. Stryker SJ, Wolff BG, Culp CE, Libbe SD, Ilstrup DM, MacCarty RL. Natural history of untreated colonic polyps. *Gastroenterology.* 1987;93(5):1009-1013.

5. Rustgi AK. Hereditary gastrointestinal polyposis and nonpolyposis syndromes. *N Engl J Med.* 1994;331:1694-1702.

6. Fuchs CS, Giovannucci EL, Colditz GA, Hunter DJ, Speizer FE, Willett WC. A prospective study of family history and the risk of colorectal cancer. *N Engl J Med.* 1994;331:1669-1674.

7. Eaden JA, Mayberry JF. Colorectal cancer complicating ulcerative colitis: a review. *Am J Gastroenterol.* 2000; 95:2710-2719.

8. Winawer SJ, Zauber AG, Gerdes H, et al. Risk of colorectal cancer in the families of patients with adenomatous polyps. National Polyp Study Workgroup. *N Engl J Med.* 1996;334:82-87.

9. Eisen GM, Sandler RS. Are women with breast cancer more likely to develop colorectal cancer? Critical review and meta-analysis. *J Clin Gastroenterol.* 1994;19: 57-63.

10. Weinberg DS, Newschaffer CJ, Topham A. Risk for colorectal cancer after gynecologic cancer. *Ann Intern Med.* 1999;131:189-193.

11. Rex D. Should we colonoscope women with gynecologic cancer? *Am J Gastroenterol.* 2000;95: 812-813.

12. Thune I. Assessments of physical activity and cancer risk. *Eur J Cancer Prev.* 2000;9:387-393.

13. Lipkin M, Reddy B, Newmark H, Lamprecht SA. Dietary factors in human colorectal cancer. *Annu Rev Nutr.* 1999;19:545-586.

14. Pignone MP, Rich M, Teutsch SM, Berg AO, Lohr KN. Rockville, Md: AHRQ; 2001.

15. Pignone M, Saha S, Hoerger T, Krages K, Helfand M, Mandelblatt J. Report submitted to the Agency for Healthcare Research and Quality. 2001.

16. U.S. Preventive Services Task Force. Guide to Clinical Preventive Services. 2nd ed. Alexandria, Va: International Medical Publishing; 1996.

17. Harris RP, Helfand M, Woolf SH, et al. Current Methods of the US Preventive Services Task Force: A Review of the Process. *Am J Prev Med.* 2001;2 (3S):forthcoming.

18. Herrinton LJ, Selby JV, Friedman GD, Quesenberry CP, Weiss NS. Case-control study of digital-rectal screening in relation to mortality from cancer of the distal rectum. *Am J Epidemiol.* 1995;142:961-964.

19. Bini EJ, Rajapaksa RC, Weinshel EH. The findings and impact of nonrehydrated guaiac examination of the rectum (FINGER) study: a comparison of 2 methods of screening for colorectal cancer in asymptomatic average-risk patients. *Arch Intern Med.* 1999;159:2022-2026.

20. Eisner MS, Lewis JH. Diagnostic yield of a positive fecal occult blood test found on digital rectal examination. Does the finger count? *Arch Intern Med.* 1991;151:2180-2184.

21. Ransohoff DF, Lang CA. Screening for colorectal cancer with the fecal occult blood test: a background paper. American College of Physicians . *Annals of Internal Medicine.* 1997;126:811-22.

22. Walter SD. Estimation of test sensitivity and specificity when disease confirmation is limited to positive results. *Epidemiol.* 1999;10:67-72.

23. Wagner J, Tunis S, Brown M, Ching A, Almeida R. Cost-effectiveness of colorectal

cancer screening in average-risk adults. In: Young G, Rozen P, Levin B, eds. *Prevention and Early Detection of Colorectal Cancer*. London: Saunders; 1996:321-356.

24. Mandel J, Bond J, Church T, et al. Reducing mortality from colorectal cancer by screening for fecal occult blood. *N Engl J Med.* 1993;328:1365-1371.

25. Mandel JS, Church TR, Bond JH, et al. The effect of fecal occult-blood screening on the incidence of colorectal cancer. *N Engl J Med.* 2000;343:1603-1607.

26. Hardcastle J, Chamberlain J, Robinson M, et al. Randomised controlled trial of faecal-occult-blood screening for colorectal cancer. *Lancet.* 1996;348:1472-1477.

27. Kronborg O, Fenger C, Olsen J, Jorgensen D, Sondergaard O. Randomised study of screening for colorectal cancer with faecal-occult-blood test. *Lancet.* 1996;348:1467-1471.

28. Eddy DM. Screening for colorectal cancer. *Ann Intern Med.* 1990;113:373-384.

29. Ahlquist DA, Skoletsky JE, Boynton KA, et al. Colorectal cancer screening by detection of altered human DNA in stool: feasibility of a multitarget assay panel. *Gastroenterology.* 2000;119:1219-1227.

30. Mandel JS, Church TR, Ederer F, Bond JH. Colorectal cancer mortality: effectiveness of biennial screening for fecal occult blood . *J Natl Cancer Inst.* 1999;91:434-437.

31. Towler B, Irwig L, Glasziou P, Kewenter J, Weller D, Silagy C. A systematic review of the effects of screening for colorectal cancer using the faecal occult blood test, Hemoccult. *BMJ.* 1998;317:559-565.

32. Vernon SW. Participation in colorectal cancer screening: a review. *J Natl Cancer Inst.* 1997;89:1406-1422.

33. Balas EA, Weingarten S, Garb CT, Blumenthal D, Boren SA, Brown GD. Improving preventive care by prompting physicians. *Arch Intern Med.* 2000;160:301-308.

34. Pignone M, Bucholtz D, Harris R. Patient preferences for colon cancer screening. *J Gen Intern Med.* 1999;14:432-437.

35. Lieberman DA, Weiss DG, Bond JH, Ahnen DJ, Garewal H, Chejfec G. Use of colonoscopy to screen asymptomatic adults for colorectal cancer. Veterans Affairs Cooperative Study Group 380. *N Engl J Med.* 2000;343:162-168.

36. Imperiale TF, Wagner DR, Lin CY, Larkin GN, Rogge JD, Ransohoff DF. Risk of advanced proximal neoplasms in asymptomatic adults according to the distal colorectal findings. *N Engl J Med.* 2000;343:169-174.

37. Atkin WS, Hart A, Edwards R, et al. Uptake, yield of neoplasia, and adverse effects of flexible sigmoidoscopy screening. *Gut.* 1998;42:560-565.

38. Lehman GA, Buchner DM, Lappas JC. Anatomical extent of fiberoptic sigmoidoscopy. *Gastroenterology.* 1983;84:803-808.

39. Thiis-Evensen E, Hoff GS, Sauar J, Langmark F, Majak BM, Vatn MH. Population-based surveillance by colonoscopy: effect on the incidence of colorectal cancer: Telemark Poly Study I. *Scand J Gastroenterol.* 1999;34:414-420.

40. Kramer BS, Gohagan J, Prorok PC, Smart C. A National Cancer Institute sponsored screening trial for prostatic, lung, colorectal, and ovarian cancers. *Cancer.* 1993;71:589-593.

41. Selby J, Friedman G, Quesenberry C, Weiss N. A case-control study of screening sigmoidoscopy and mortality from colorectal cancer. *N Engl J Med.* 1992;326:653-657.

42. Newcomb PA, Norfleet RG, Storer BE, Surawicz TS, Marcus PM. Screening sigmoidoscopy and colorectal cancer mortality. *J Natl Cancer Inst.* 1992;84:1572-1575.

43. Nelson RL, Abcarian H, Prasad ML. Iatrogenic perforation of the colon and rectum. *Dis Colon Rectum.* 1982;25:305-308.

44. Anderson JC, Pollack BJ, Shaw RD. Virtual colonoscopy. *N Engl J Med.* 2000;342:738; discussion 738-739.

45. Verne JE, Aubrey R, Love SB, Talbot IC, Northover JM. Population based randomized study of uptake and yield of screening by flexible sigmoidoscopy compared with screening by faecal occult blood testing. *BMJ.* 1998;317:182-185.

46. Schoen RE, Weissfeld JL, Bowen NJ, Switzer G, Baum A. Patient satisfaction with screening flexible sigmoidoscopy. *Arch Intern Med.* 2000;160:1790-1796.

47. Winawer S. Screening for colorectal cancer with fecal occult blood testing and sigmoidoscopy. *J Natl Cancer Inst.* 1993;85(16):1311-1318.

48. Berry DP, Clarke P, Hardcastle JD, Vellacott KD. Randomized trial of the addition of flexible sigmoidoscopy to faecal occult blood testing for colorectal neoplasia population screening. *Br J Surg.* 1997;84:1274-1276.

49. Rasmussen M, Kronborg O, Fenger C, Jorgensen OD. Possible advantages and drawbacks of adding flexible sigmoidoscopy to hemoccult-II in screening for colorectal cancer: a randomized study. *Scand J Gastroenterol.* 1999;34:73-78.

50. Ott DJ, Scharling ES, Chen YM, Wu WC, Gelfand DW. Barium enema examination: sensitivity in detecting colonic polyps and carcinomas. *South Med J.* 1989;82:197-200.

51. Beggs I, Thomas BM. Diagnosis of carcinoma of the colon by barium enema. *Clin Radiol.* 1983;34:423-425.

52. Rex DK, Rahmani EY, Haseman JH, Lemmel GT, Kaster S, Buckley JS. Relative sensitivity of colonoscopy and barium enema for detection of colorectal cancer in clinical practice. *Gastroenterology.* 1997;112:17-23.

53. Johnson CD, Carlson HC, Taylor WF, Weiland LP. Barium enemas of carcinoma of the colon: sensitivity of double- and single-contrast studies. *Am J Roentgenology.* 1983;140:1143-1149.

54. Bloomfield JA. Reliability of barium enema in detecting colonic neoplasia. *Med J Aust.* 1981;1:631-633.

55. Teefey SA, Carlson HC. The fluoroscopic barium enema in colonic polyp detection. *Am J Roentgenology.* 1983;141:1279-1281.

56. Brady AP, Stevenson GW, Stevenson I. Colorectal cancer overlooked at barium enema examination and colonoscopy: a continuing perceptual problem. *Radiology.* 1994;192:373-378.

57. Strom E, Larsen JL. Colon cancer at barium enema examination and colonoscopy: a study from the county of Hordaland, Norway. *Radiology.* 1999;211:211-214.

58. Brekkan A, Kjartansson O, Tulinius H, Sigvaldason H. Diagnostic sensitivity of X-ray examination of the large bowel in colorectal cancer. *Gastrointest Radiol.* 1983;8:363-365.

59. Glick S, Wagner JL, Johnson CD. Cost-effectiveness of double-contrast barium enema in screening for colorectal cancer. *Am J Roentgenology.* 1998;170:629-636.

60. Myllyla V, Paivansalo M, Laitinen S. Sensitivity of single and double contrast barium enema in the detection of colorectal carcinoma. *Rofo: Fortschritte Auf Dem Gebiete Der Rontgenstrahlen Und Der Nuklearmedizin.* 1984;140:393-397.

61. Winawer SJ, Stewart ET, Zauber AG, et al. A comparison of colonoscopy and double-contrast barium enema for surveillance after polypectomy. *N Engl J Med.* 2000;342(24):1766-1772.

62. 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;329:1977-1981.

63. Kewenter J, Brevinge H. Endoscopic and surgical complications of work-up in screening for colorectal cancer. *Dis Colon Rectum.* 1996;39:676-680.

64. Blakeborough A, Sheridan MB, Chapman AH. Complications of barium enema examinations: a survey of UK Consultant Radiologists 1992 to 1994. *Clin Radiol.* 1997;52:142-148.

65. Steine S. Which hurts the most? A comparison of pain rating during double-contrast barium enema examination and colonoscopy. *Radiology.* 1994;191:99-101.

66. Van Ness MM, Chobanian SJ, Winters C Jr, Diehl AM, Esposito RL, Cattau EL Jr. A study of patient acceptance of double-contrast barium enema and colonoscopy. Which procedure is preferred by patients? *Arch Intern Med.* 1987;147:2175-2176.

67. Newcomer MK, Shaw MJ, Williams DM, Jowell PS. Unplanned work absence following outpatient colonoscopy. *J Clin Gastroenterology.* 1999;29:76-78.

68. Rex DK, Cutler CS, Lemmel GT, et al. Colonoscopic miss rates of adenomas determined by back-to-back colonoscopies. *Gastroenterology.* 1997;112:24-28.

69. Rembacken BJ, Fujii T, Cairns A, et al. Flat and depressed colonic neoplasms: a prospective study of 1000 colonoscopies in the UK. *Lancet.* 2000;355:1211-1214.

70. Muller AD, Sonnenberg A. Protection by endoscopy against death from colorectal cancer. A case-control study among veterans. *Arch Intern Med.* 1995;155:1741-1748.

71. Frazier AL, Colditz GA, Fuchs CS, Kuntz KM. Cost-effectiveness of screening for colorectal cancer in the general population. *JAMA.* 2000;284:1954-1961.

72. Eckardt VF, Kanzler G, Schmitt T, Eckardt AJ, Bernhard G. Complications and adverse effects of colonoscopy with selective sedation. *Gastrointest Endosc.* 1999;49:560-565.

73. Zubarik R, Fleischer DE, Mastropietro C, et al. Prospective analysis of complications 30 days after outpatient colonoscopy. *Gastrointest Endosc.* 1999;50:322-328.

74. Wexner SD, Forde KA, Sellers G, et al. How well can surgeons perform colonoscopy? *Surg Endosc.* 1998;12:1410-1414.

75. Farley DR, Bannon MP, Zietlow SP, Pemberton JH, Ilstrup DM, Larson DR. Management of colonoscopic perforations. *Mayo Clinic Proc.* 1997;72:729-733.

76. Foliente RL, Chang AC, Youssef AI, Ford LJ, Condon SC, Chen YK. Endoscopic cecal perforation: mechanisms of injury. *Am J Gastroenterol.* 1996;91:705-708.

77. Gibbs DH, Opelka FG, Beck DE, Hicks TC, Timmcke AE, Gathright JBJ. Postpolypectomy colonic hemorrhage. *Dis Colon Rectum.* 1996;39:806-810.

78. Ure T, Dehghan K, Vernava AM III, Longo WE, Andrus CA, Daniel GL. Colonoscopy in the elderly. Low risk, high yield. *Surg Endosc.* 1995;9:505-508.

79. Lo AY, Beaton HL. Selective management of colonoscopic perforations. *J Am Coll Surg.* 1994;179:333-337.

80. Rosen L, Bub DS, Reed JF III, Nastasee SA. Hemorrhage following colonoscopic polypectomy. *Dis Colon Rectum.* 1993;36:1126-1131.

81. DiPrima RE, Barkin JS, Blinder M, Goldberg RI, Phillips RS. Age as a risk factor in colonoscopy: fact versus fiction. *Am J Gastroenterol.* 1988;83:123-125.

82. Nivatvongs S. Complications in colonoscopic polypectomy: lessons to learn from an experience with 1576 polyps. *Am Surg.* 1988;54:61-63.

83. Brynitz S, Kjaergard H, Struckmann J. Perforations from colonoscopy during diagnosis and treatment of polyps. *Annales Chirurgiae Et Gynaecologiae.* 1986;75:142-145.

84. Webb WA, McDaniel L, Jones L. Experience with 1000 colonoscopic polypectomies. *Ann Surg.* 1985;201:626-632.

85. Macrae FA, Tan KG, Williams CB. Towards safer colonoscopy: a report on the complications of 5000 diagnostic or therapeutic colonoscopies. *Gut.* 1983;24:376-383.

86. Leard L, Savides T, Ganiats T. Patient preferences for colorectal cancer screening. *J Fam Pract.* 1997;45:211-218.

87. Halligan S, Fenlon HM. Science, medicine, and the future: virtual colonoscopy. *BMJ.* 1999;319:1249-1252.

88. Pescatore P, Glucker T, Delarive J, et al. Diagnostic accurarcy and interobserver agreement of CT colonography (virtual colonoscopy). *Gut.* 2000;47:126-130.

89. Pignone MP, Saha S, Hoerger T, Mandelblatt J, Krages K, Helfand M. *Systematic Review of Cost-Effectiveness Analyses for Colorectal Cancer Screening*. Rockville, Md: Agency for Healthcare Research and Quality; forthcoming.

90. Khandker RK, Dulski JD, Kilpatrick JB, Ellis RP, Mitchell JB, Baine WB. A decision model and cost-effectiveness analysis of colorectal cancer screening and surveillance guidelines for average-risk adults. *Int J Technol Assess Health Care.* 2000;16:799-810.

91. Sonnenberg A, Delco F, Inadomi JM. Cost-effectiveness of colonoscopy in screening for colorectal cancer. *Ann Intern Med.* 2000;133:573-584.

Figure 1. Cancers of the Colon and Rectum: Average Annual Age-Specific SEER Incidence per 100,000 Persons and U.S. Mortality Rates By Gender, 1992-1996

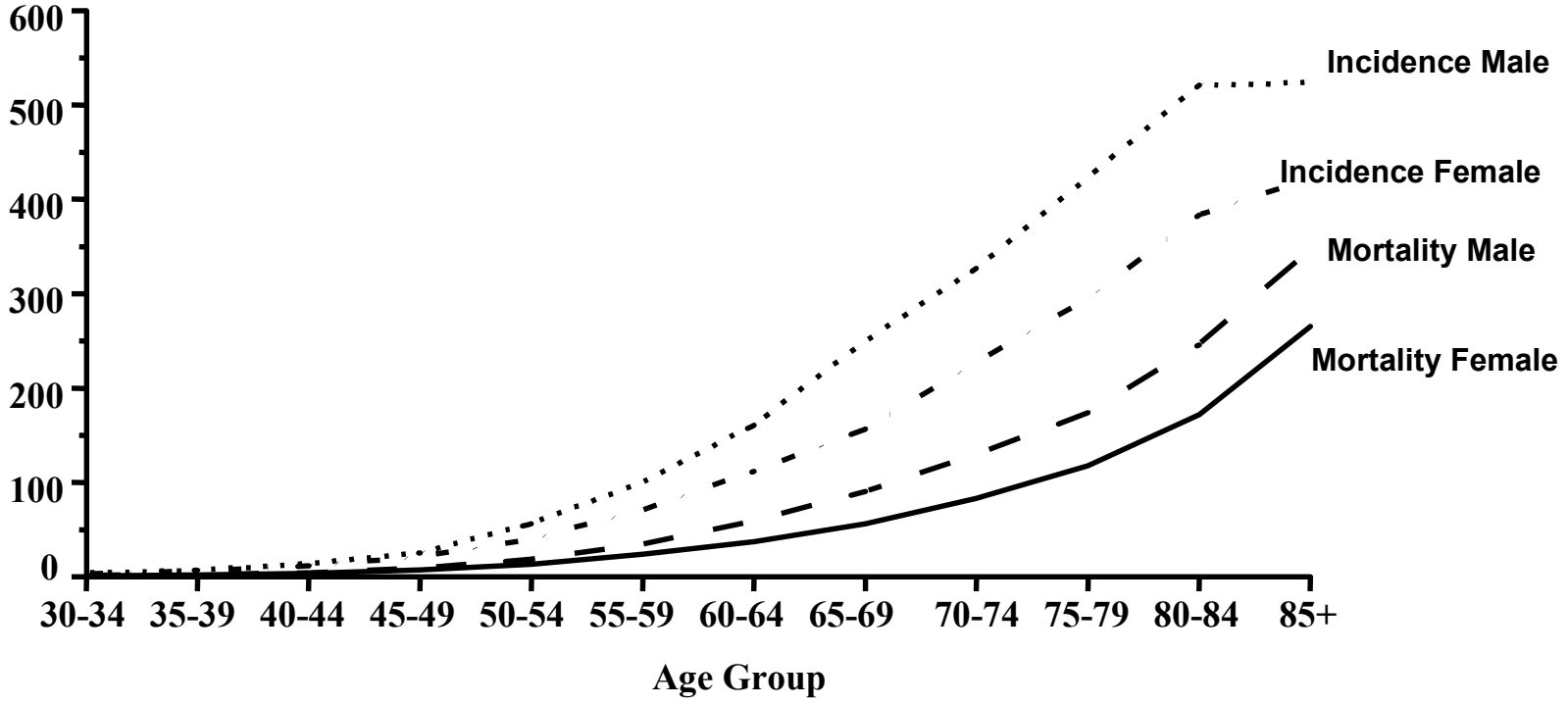
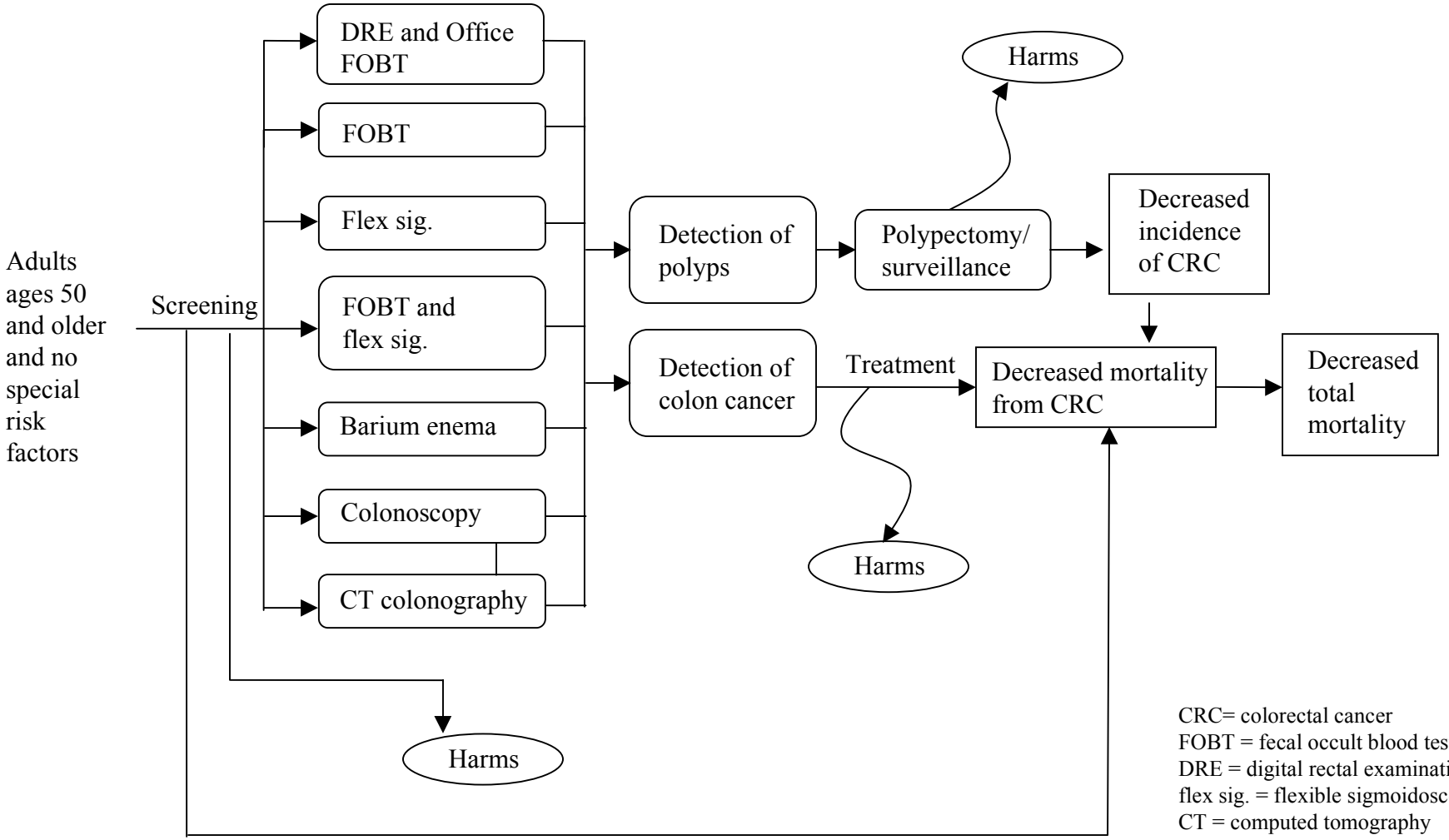


Figure 2. Colorectal Cancer (CRC) Screening: Analytic Framework



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PRE-ASSESSMENT Virtual Colonoscopy

Before CCOHTA decides to undertake a health technology assessment, a pre-assessment of the literature is performed. Pre-assessments are based on a limited literature search; they are not extensive, systematic reviews of the literature. They are provided here as a quick guide to important, current assessment information on this topic. Readers are cautioned that the pre-assessments have not been externally peer reviewed.

Introduction

In Canada, colorectal cancer is the fourth most commonly diagnosed cancer and the second most common cause of cancer-related mortality. An estimated 18,000 new cases and 8,300 deaths from colorectal cancer occurred in Canada in 2003.[1] The prognosis and survival of those with colorectal cancer are related to the stage of the cancer at the time of diagnosis. This disease is treatable and often curable if the cancer is localized. Early detection of colorectal cancer through screening (secondary prevention) can reduce the mortality and morbidity associated with this disease.[2]

Several approaches to screening are available, ranging from the least expensive and least invasive (fecal occult blood testing) to the more costly and invasive procedures (flexible sigmoidoscopy, barium enema and colonoscopy). Each of these tests has inherent strengths and weaknesses related to cost, risk, sensitivity, specificity and availability.[2,3] Colonoscopy, which is considered to be the gold standard, is an invasive test that must be performed by an experienced specialist. It carries risks of bleeding, the required sedatives cause side effects and there are other associated complications. Some patients complain that the bowel-cleansing preparation is worse than the procedure itself.[3]

Virtual colonoscopy (VC) was first described in 1994 as a non-invasive test for the examination of the colonic lumen for cancers and polyps.[2,3] The term VC is used interchangeably with computed tomographic colonography (CTC) and magnetic resonance colonography. The latter technique uses magnetic resonance imaging, but thus far, CTC has been studied and used more extensively.[4]

CTC requires the same bowel-cleansing preparation as colonoscopy. The insertion of a rectal tube and the insufflation of air or carbon dioxide are required to distend the colon.[2] Sedation is unnecessary. The time required for the procedure is approximately five to 15 minutes, plus an additional 15 to 40 minutes for interpretation.[2] Typically, two-dimensional computed tomographic (CT) images can be processed with the use of commercially available software programs to render a three-dimensional display of the colonic lumen. Virtual images of the entire colon can be examined segment by segment, much as they are during colonoscopy.[3]

The Canadian Coordinating Office for Health Technology Assessment (CCOHTA) published a pre-assessment of CTC in October 2002 concluding that: “Several other HTA agencies have recently assessed virtual colonoscopy and others have work underway. At this point, CCOHTA will not duplicate these efforts and will wait until further evidence becomes available.”[4] This topic was subsequently forwarded by a

consumer through CCOHTA's web site, for consideration as an assessment, to CCOHTA's Devices and Systems Advisory Committee (DSAC) in September 2003. The DSAC selected this topic for assessment as an update to the October 2002 pre-assessment.

Research Question

How does CTC compare with conventional technologies that image the colon?

Assessment Process

PubMed was searched using controlled vocabulary and key words for "virtual colonoscopy" and "controlled trials" or "comparative studies." Retrieval was limited to the human population (this limit was not applied to publisher-supplied or in-process citations). The Cochrane Library 2004 issue 1 was also searched. Grey literature was obtained through searching the web sites of health technology assessment and related agencies; and their associated databases. Google™ was used to search for additional web-based information. Correspondence was initiated with the Medical Advisory Secretariat of the Ministry of Health and Long-Term Care in Ontario to determine the status of its ongoing evaluation. A draft of the Ontario report dated October 2003 was given to CCOHTA.

Summary of Findings

Reviews or Meta-analysis

Two reviews published since the October 2002 pre-assessment were identified: the draft Ontario report (October 2003) and a meta-analysis on CT of colorectal polyps published in the *American Journal of Radiology* in December 2003[5] (Table 1).

Table 1: Summary of findings

Title (Author, Year)	Objective(s)	Methods	Results	Conclusions
Computed tomographic colonography (virtual colonoscopy) (Medical Advisory Secretariat, Ontario, draft, October 2003)	To compare effectiveness and safety of CTC as a screening method for detection of colon cancer and pre-cancerous polyps with	Literature search on MEDLINE and EMBASE for English language studies from 2000 to May 2003	18 studies of 2,017 patients, of whom 126 (6%) were asymptomatic. Performance of CTC depends on size of lesions. Sensitivity ranges for multi-slice versus single-slice scanning: 86% to 100% versus	With limited sensitivity and specificity of CTC relative to colonoscopy; and lack of therapeutic intervention,CTC may result in inconve-nience, cost and complications.

	reference standard of conventional colonoscopy		67% to 100% for cancer detection; 80% to 100% versus 57% to 100% for polyps >10 mm; 33% to 86% versus 0% to 80% for polyps 6 mm to 9 mm; 3% to 70% versus 10% to 68% for polyps ≤5 mm. Diagnostic performance of CTC depends on methods of bowel preparation, adequate bowel distension and scanning techniques.	Based on current evidence, CTC cannot be proposed for routine population-based screening for polyps or cancer. Patients with colonic symptoms or history of polyps will benefit more if they undergo colonoscopy including excision of premalignant polyps. CTC can be the examination of choice for preoperative evaluation of patients with colorectal carcinomas, given its possibility of assessing entire colon, extracolonic structures and tumour staging. CTC can be considered for diagnostic purposes when colonoscopy is clinically contraindicated or when patients had incomplete colonoscopy because of stenosis or obstruction of colon. MRI-based VC that excludes risk of ionizing radiation may be of more benefit than CTC in the future.

CT Colonography of Colorectal Cancer: A Meta-analysis (Sosna, December 2003)[5]	To assess reported accuracy of CTC compared to conventional colonoscopy for detecting colorectal polyps	Literature search on PubMed and MEDLINE for English language studies from 1994 to July 2002	14 studies of 1,324 patients (1,411 polyps).[2] Pooled per-patient sensitivity (95% CI): 88% (0.84 to 0.93) for polyps >10 mm; 84% (0.80 to 0.89) for 6 mm to 9 mm; 65% (0.57 to 0.73) for polyps ≤5 mm. Sensitivity for detection of polyps increased as polyp size increased (p<0.0001). Pooled specificity for polyps >10 mm was 0.95 (0.94 to 0.97).	Specificity and sensitivity of CTC are high for polyps >10 mm.

[1] Two additional studies published since original literature search are being incorporated in Ontario report.
[2] All nine studies published in 2000 to 2002 were included in Ontario report.

Primary studies

In comparison to the studies included in the two reviews above, the literature search identified an additional eight diagnostic accuracy studies,[6-13] two studies on cost or cost-effectiveness[14,15] and five studies on patients' acceptance of CTC.[16-20]

a) Diagnostic studies

Two of the largest diagnostic studies[7,11] identified for this pre-assessment are being incorporated in the Ontario report. Pickhardt *et al.* report the largest prospective evaluation to date of CTC as a colorectal screening test. The study involved 1,233 asymptomatic adults who underwent CTC and same-day conventional colonoscopy.[11] More than 97% of the subjects were at average risk for colorectal cancer. The sensitivity of CTC was 92% for polyps of ≥10 mm, 93% for polyps of ≥8 mm and 86% for polyps of ≥6 mm, as compared with 88%, 89.5% and 90% respectively for colonoscopy performed by colonoscopists who were blinded to the CTC test results.[11] The negative predictive value of normal findings on CTC was >99% for polyps of ≥8 mm. If a threshold polyp size of 10 mm had been used, for example, 7.5% of patients who underwent CTC would have required referral for polypectomy. The average time spent by patients undergoing CTC was 14 minutes (approximately half that required for colonoscopy) and the average time required for the interpretation of CTC studies was <20 minutes.[11] Several factors may explain these impressive results by Pickhardt *et al.* They used a different technique from that used in previous studies. It enabled the imaging software to digitally remove all opaque fluid and stool from the image

by a process known as electronic cleansing. They used multi-detector CT scanners, which permitted faster higher-resolution imaging than single-detector scanners that had been used previously. The calculation of CTC sensitivity was based only on adenomas with the exclusion of non-adenomatous polyps as false positive results.

The second largest study being incorporated in the Ontario report is by Johnson *et al.* This study consists of 703 asymptomatic patients reporting on polyp detection rates at CTC being below those at colonoscopy with high inter-observer variability of CTC test results among three experienced readers.[7] The remaining six studies reporting on conflicting findings include a small sample size (range of 23 to 205 subjects) and consist of symptomatic and asymptomatic patients.[6,8-10,12,13]

b) Cost and cost-effectiveness studies

Two studies examined the cost or cost-effectiveness of CTC in comparison to colonoscopy screening. McGrath, using a decision analytic model based on Ontario cost data, reported on the cost of finding an advanced adenoma in patients undergoing flexible sigmoidoscopy, colonoscopy and CTC.[14] Colonoscopy was less costly and detected more cases of advanced adenomas in comparison with the other two screening strategies.[14] Sonnenberg, using computer models based on a Markov process, found screening by colonoscopy to remain more cost-effective even if the sensitivity and specificity of CTC both rose to 100%. To become cost-effective, CT or magnetic resonance colonography would have to be offered at a low price or result in compliance rates that are better than those associated with colonoscopy.[15]

c) Patient acceptance for CTC

Five studies reported on patients' acceptance and preferences for CTC. Four studies reported an overall preference by patients for CTC in comparison with colonoscopy for follow-up examinations.[17-20] Patients in the study by Akerkar, despite tolerating both CTC and colonoscopy, reported more pain, discomfort and less respect undergoing CTC.[16]

Conclusion

As a review is being undertaken by the Ministry of Health and Long-Term Care in Ontario, CCOHTA will not undertake an assessment on CTC at this time.

References

1. National Cancer Institute of Canada, Canadian Cancer Society. *Canadian cancer statistics 2003*. Toronto: The Society; 2003. Available: http://www.cancer.ca/vgn/images/portal/cit_776/61/38/56158640niw_stats_en.pdf (accessed 2003 Apr 28).

2. Walsh JM, Terdiman JP. Colorectal cancer screening: scientific review. *JAMA* 2003;289(10):1288-96.

3. Morrin MM, LaMont JT. Screening virtual colonoscopy--ready for prime time? *N Engl J Med* 2003;349(23):2261-4.

4. Topfer L-A. *Virtual colonoscopy (computed tomography colonography)* [Pre-assessment no. 9]. Ottawa: Canadian Coordinating Office for Health Technology Assessment; 2002. Available: http:/www.ccohta.ca (accessed 2003 Nov 17).

5. Sosna J, Morrin MM, Kruskal JB, Lavin PT, Rosen MP, Raptopoulos V. CT colonography of colorectal polyps: a metaanalysis. *Am J Roentgenol* 2003;181(6):1593-8.

6. Iannaccone R, Laghi A, Catalano C, Brink JA, Mangiapane F, Trenna S, et al. Detection of colorectal lesions: lower-dose multi-detector row helical CT colonography compared with conventional colonoscopy. *Radiology* 2003;229(3):775-81.

7. Johnson CD, Harmsen WS, Wilson LA, Maccarty RL, Welch TJ, Ilstrup DM, et al. Prospective blinded evaluation of computed tomographic colonography for screen detection of colorectal polyps. *Gastroenterology* 2003;125(2):311-9.

8. Macari M, Bini EJ, Jacobs SL, Naik S, Lui YW, Milano A, et al. Colorectal polyps and cancers in asymptomatic average-risk patients: evaluation with CT colonography. *Radiology* 2004;230(3):629-36.

9. Munikrishnan V, Gillams AR, Lees WR, Vaizey CJ, Boulos PB. Prospective study comparing multislice CT colonography with colonoscopy in the detection of colorectal cancer and polyps. *Dis Colon Rectum* 2003;46(10):1384-90.

10. Ginnerup Pedersen B, Christiansen TE, Bjerregaard NC, Ljungmann K, Laurberg S. Colonoscopy and multidetector-array computed-tomographic colonography: detection rates and feasibility. *Endoscopy* 2003;35(9):736-42.

11. Pickhardt PJ, Choi JR, Hwang I, Butler JA, Puckett ML, Hildebrandt HA, et al. Computed tomographic virtual colonoscopy to screen for colorectal neoplasia in asymptomatic adults. *N Engl J Med* 2003;349(23):2191-200.

12. Pineau BC, Paskett ED, Chen GJ, Espeland MA, Phillips K, Han JP, et al. Virtual colonoscopy using oral contrast compared with colonoscopy for the detection of patients with colorectal polyps. *Gastroenterology* 2003;125(2):304-10.

13. Xynopoulos D, Stasinopoulou M, Dimitroulopoulos D, Tsamakides K, Arhavlis E, Kontou M, et al. Colorectal polyp detection with virtual colonoscopy (computed tomographic colonography); the reliability of the method. *Hepatogastroenterology* 2002;49(43):124-7.

14. McGrath JS, Ponich TP, Gregor JC. Screening for colorectal cancer: the cost to find an advanced adenoma. *Am J Gastroenterol* 2002;97(11):2902-7.

15. Sonnenberg A, Delcò F, Bauerfeind P. Is virtual colonoscopy a cost-effective option to screen for colorectal cancer? *Am J Gastroenterol* 1999;94(8):2268-74.

16. Akerkar GA, Yee J, Hung R, McQuaid K. Patient experience and preferences toward colon cancer screening: a comparison of virtual colonoscopy and conventional colonoscopy. *Gastrointest Endosc* 2001;54(3):310-5.

17. Ristvedt SL, McFarland EG, Weinstock LB, Thyssen EP. Patient preferences for CT colonography, conventional colonoscopy, and bowel preparation. *Am J Gastroenterol* 2003;98(3):578-85.

18. Svensson MH, Svensson E, Lasson A, Hellström M. Patient acceptance of CT colonography and conventional colonoscopy: prospective comparative study in patients with or suspected of having colorectal disease. *Radiology* 2002;222(2):337-45.

19. Taylor SA, Halligan S, Saunders BP, Bassett P, Vance M, Bartram CI. Acceptance by patients of multidetector CT colonography compared with barium enema examinations, flexible sigmoidoscopy, and colonoscopy. *Am J Roentgenol* 2003;181(4):913-21.

20. Thomeer M, Bielen D, Vanbeckevoort D, Dymarkowski S, Gevers A, Rutgeerts P, et al. Patient acceptance for CT colonography: What is the real issue? *Eur Radiol* 2002;12(6):1410-5.

Computed Tomography Colonography

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MSAC application 1095

Assessment Report

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Electronic copies of the report can be obtained from the Medical Service Advisory Committee's Internet site at http://www.msac.gov.au/

Printed copies of the report can be obtained from:

The Secretary
Medical Services Advisory Committee
Department of Health and Ageing
Mail Drop 106
GPO Box 9848
Canberra ACT 2601

Enquiries about the content of the report should be directed to the above address.

The Medical Services Advisory Committee (MSAC) is an independent committee which has been established to provide advice to the Minister for Health and Ageing on the strength of evidence available on new and existing medical technologies and procedures in terms of their safety, effectiveness and cost-effectiveness. This advice will help to inform government decisions about which medical services should attract funding under Medicare.

MSAC recommendations do not necessarily reflect the views of all individuals who participated in the MSAC evaluation.

This report was prepared by the Medical Services Advisory Committee with the assistance of Silke Walleser, Sarah Lord, Alison Griffiths, Kirsten Howard and Alisa Higgins, from the NHMRC Clinical Trials Centre. The report was edited by Bruce Howarth. The report was endorsed by the Minister for Health and Ageing on 24 August 2006.

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Contents

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Figures

Executive summary

The procedure

Computed tomography colonography (CTC) is a minimally invasive radiological technique for imaging the colon and rectum. It involves the use of a spiral CT scanner to acquire multiple simultaneous tomographic sections ('slices') of the colon and rectum during one rotation of the x-ray source. A computer software program reformats these data to produce two dimensional images or three-dimensional reconstructions of the bowel (also referred to as 'virtual colonoscopy'). Patients require a bowel preparation the day before the procedure. At the time of scanning, the colon is insufflated with air or carbon dioxide via a catheter placed in the rectum. The patient does not require sedation.

Medical Services Advisory Committee – role and approach

The Medical Services Advisory Committee (MSAC) was established by the Australian Government to strengthen the role of evidence in health financing decisions in Australia. MSAC advises the Minister for Health and Ageing on the evidence relating to the safety, effectiveness and cost-effectiveness of new and existing medical technologies and procedures, and under what circumstances public funding should be supported.

A rigorous assessment of evidence is thus the basis of decision making when funding is sought under Medicare. A team from the NHMRC Clinical Trials Centre was engaged to conduct a systematic review of literature on CTC. An advisory panel with expertise in this area then evaluated the evidence and provided advice to MSAC.

MSAC's assessment of computed tomography colonography

Clinical need

Colorectal cancer is the most common cancer (excluding non-melanoma skin cancer) and the third most common cause of cancer death reported to Australian cancer registries. In 2001, there were 12,844 new cases of colorectal cancer reported and 4,754 deaths, accounting for 14.5% of all new cases of cancer and 13.1% of cancer deaths (Australian Institute of Health & Welfare (AIHW) & Australasian Association of Cancer Registries (AACR) 2004).

CTC has been proposed as a minimally invasive alternative to double contrast barium enema (DCBE) and colonoscopy in patients requiring investigation or surveillance for the detection of colorectal neoplasia (cancers and polyps). CTC does not allow biopsy like colonoscopy, but can be used in patients in whom colonoscopy is contraindicated or cannot be completed.

Reimbursement for CTC has been available as an interim item under the Medicare Benefits Schedule since May 2005 for two indications: (i) following an incomplete colonoscopy; and (ii) in patients with fistulous disease, obstructed colon, or megacolon in whom colonoscopy is contraindicated. Over the 6-month period, May to October 2005, 665 CTC were billed under these items in Australia with a trend of increasing CTC

requests over this period. This figure does not include the number of CTCs performed for other indications, nor the number of CTCs performed on public patients treated in public hospitals. It is difficult to estimate the potential magnitude of CTC use should it be funded for the diagnosis or exclusion of colorectal neoplasia under wider indications because data about the number of DCBE and colonoscopies performed in Australia each year do not record the indication for testing.

Review methods

This review addresses two research questions to determine the potential value of CTC for the diagnosis or exclusion of colorectal neoplasia in Australia.

Review question 1

What is the safety, effectiveness and cost-effectiveness of CTC versus DCBE and versus colonoscopy for the diagnosis or exclusion of colorectal neoplasia in symptomatic patients or in patients that are asymptomatic but at high risk of colorectal neoplasia due to a personal or family history of colorectal polyps or cancer?

Review question 2

What is the safety, effectiveness and cost-effectiveness of CTC versus DCBE for the diagnosis or exclusion of colorectal neoplasia in symptomatic or high-risk patients who are ineligible for colonoscopy due to patient contraindications or the inability to perform or complete the test?

Secondary analyses were conducted to assess the safety, effectiveness and cost-effectiveness of CTC versus DCBE and versus colonoscopy to detect other specific colorectal abnormalities and all colorectal abnormalities.

Literature search

A systematic review of the medical literature was undertaken using MEDLINE, Pre-MEDLINE, EMBASE, Current Contents, the Cochrane Library and Health Technology Assessment databases to identify relevant studies and systematic reviews published between January 1994 and June 2005.

This search did not identify any studies comparing overall health outcomes following the use of CTC, DCBE or colonoscopy. Conclusions about the safety and effectiveness of CTC are based on four systematic reviews and 24 clinical studies that reported on CTC and/or DCBE safety and accuracy with or without comparisons with colonoscopy and 11 studies that reported on patient preferences or quality of life outcomes associated with these tests.

Safety

CTC is a relatively safe procedure compared to DCBE and as least as safe as, or safer than, diagnostic colonoscopy. Both CTC and DCBE expose patients to ionizing radiation and are associated with a very small risk of colonic perforation.

Effectiveness

CTC accuracy

CTC is generally highly sensitive and specific for the diagnosis or exclusion of cancers and polyps ≥ 10 mm in symptomatic patients and asymptomatic patients at high risk of colorectal neoplasia (11 studies of variable quality, median CTC sensitivity 84% (range 55-100%); median CTC specificity 97% (range 74-100%)). Estimates of CTC accuracy are higher for the detection of cancer alone (meta-analysis of four studies: CTC sensitivity 97% (95% CI 89-100%); CTC specificity 98% (95% CI 95-99%). These findings are consistent with results from three published systematic reviews.

CTC is only moderately sensitive for the detection of lesions 6-9 mm and poorly sensitive for lesions < 5 mm (lesions 6-9 mm: six studies, CTC sensitivity range 30-80%, CTC specificity range 93-99%; lesions ≤ 5 mm: four studies, CTC sensitivity range 14-57%, CTC specificity range 83-97%).

The variation observed between studies demonstrates that CTC is less accurate in some population subgroups or settings. The extent to which patient characteristics, prevalence of disease, CTC techniques, the experience of those performing and interpreting the tests or other factors may influence CTC performance has not yet been clearly defined.

Relative accuracy of CTC, DCBE and colonoscopy

Studies comparing CTC with DCBE and colonoscopy provide the best evidence to assess the relative accuracy of these tests. This evidence was limited to one study of fair quality (Rockey et al 2005) that found CTC and DCBE accuracy to be lower than noncomparative studies and systematic reviews of CTC accuracy. This study indicated that CTC is a more specific test than DCBE, but less sensitive and specific than colonoscopy for the detection of cancers and polyps ≥ 10 mm. This study also suggested that CTC may be a more sensitive test than DCBE; this difference did not reach statistical significance for lesions ≥ 10 mm, but was shown to be statistically significant for lesions 6-9 mm.

Relative accuracy of CTC, DCBE and colonoscopy for the detection of lesions ≥ 10mm (Rockey et al 2005)

Test	Sensitivity (95% CI)	p value[1]	Specificity (95% CI)	p value[1]
CTC	59% (46-71%)		96% (94-98%)	
DCBE	48% (35-61%)	0.11	90% (87-92%)	< 0.0001
colonoscopy	98.3% (91-100%)	< 0.0001	99.6% (99-100%)	< 0.0001

1 p value CTC versus comparator test.

Two studies of fair quality suggest that CTC may be more accurate than DCBE for the detection of all colorectal disease but less sensitive than colonoscopy; however, no studies have directly compared these tests (Munikrishnan et al 2003, Durdey et al 1987).

CTC patient preferences and quality of life

Three studies of fair to high quality have reported a statistically significant difference in patient preference, satisfaction and experience of pain or discomfort in favour of CTC versus DCBE (Gluecker et al 2003, Taylor et al 2005, Taylor et al 2003).

The evidence reviewed also suggests that CTC may be preferred over colonoscopy. However, comparison of pain and discomfort experienced by patients undergoing both tests have shown mixed results with three of eight studies reporting results in favour of colonoscopy.

Additional considerations

CTC is successful in visualising the entire colon in at least 90% of patients following an incomplete colonoscopy and may detect colorectal lesions in 18 to 27% of patients that were not identified at the initial incomplete colonoscopy (Neri et al 2002, Morrin et al 1999, Macari et al 1999, Minyue et al 2002).

CTC has an advantage over DCBE for visualising the proximal colon in patients with a distal obstruction. It also has an advantage over DCBE due to technical difficulties of coating the bowel wall with barium to conduct a DCBE following a colonoscopy.

CTC also offers the opportunity for detecting extracolonic lesions that cannot be identified at DCBE or colonoscopy. Rates of clinically significant extracolonic findings ranged between 1% and 13% in six studies reviewed. Incidental and clinically nonsignificant extra-colonic findings were reported in 19% to 63% of patients by three studies. The consequences of these findings have not been assessed. Clinically significant findings may be expected to change patient management, whereas insignificant findings may result in additional unnecessary investigations and patient distress.

No studies were designed to compare test failure rates for CTC versus DCBE and/or colonoscopy; however, the studies reviewed suggest that CTC failure rates are at least comparable to or better than DCBE and colonoscopy.

Cost-effectiveness

An economic model was developed to estimate the incremental cost-effectiveness of CTC compared to colonoscopy and compared to DCBE in the patients of interest. The analysis included one- and two-way sensitivity analyses of key parameters.

For the comparison of CTC with DCBE, the modelled analysis shows a cost per life year saved of $25,420 of CTC compared to DCBE in the base case scenario (CTC cancer sensitivity: 59%, DCBE cancer sensitivity: 48%) with cost-effectiveness widely varying in sensitivity analyses from $4,882 per life year saved to a situation where CTC is dominated by DCBE.

The base case economic analysis further indicates that CTC is less costly, but also less effective than colonoscopy. The incremental cost of colonoscopy versus CTC per life year saved is $1,659 for the base case (CTC sensitivity for cancer=59%, colonoscopy sensitivity for cancer=98%). In sensitivity analyses, the cost per life year saved for colonoscopy ranged between $13,955 and a situation where colonoscopy is more effective and associated with less costs than CTC.

The results of the economic analysis must be interpreted with caution due to uncertainties around model parameters, in particular the uncertainty around the estimates of test sensitivity for cancer.

Review Question 1: CTC versus DCBE and versus colonoscopy

CTC is a relatively safe test compared to DCBE and colonoscopy.

Evidence about CTC accuracy for the detection of cancers and polyps ≥ 10 mm compares favourably with DCBE. There is also some evidence to suggest that patients prefer CTC over DCBE. CTC is more costly than DCBE and an economic model suggests a base case incremental cost per life year saved for CTC compared to DCBE of $25,420; results of the sensitivity analysis ranged from a cost per life year saved of $4,882 for CTC compared to DCBE to a situation where CTC is dominated by DCBE (more costly and less effective).

CTC is less accurate than colonoscopy for the detection of cancers and polyps ≥ 10 mm. There is also some evidence to suggest that patients prefer CTC over colonoscopy. CTC is less costly than colonoscopy and an economic model found a base case incremental cost per life year saved of $1,659 for colonoscopy compared to CTC. The cost per life year saved for colonoscopy in sensitivity analyses ranged between $13,955 and a situation where colonoscopy is more effective and associated with less costs than CTC.

Review Question 2: CTC versus DCBE in patients with a contraindication to colonoscopy

There is little evidence for a comparison of CTC versus DCBE accuracy in patients following an incomplete colonoscopy. The evidence available indicates that CTC is successful in visualising the entire colon in at least 90% of patients following an incomplete colonoscopy. CTC also has demonstrated advantages over DCBE in visualising the proximal colon in patients with a distal obstruction, the detection of extracolonic disease, and patient preferences and tolerance of testing. Another consideration favouring the use of CTC is that it can be performed immediately after a failed colonoscopy, whereas coating the bowel wall with barium can be difficult to achieve after colonoscopy.

CTC is more costly than DCBE. An economic analysis based on a general model of CTC compared to DCBE in symptomatic patients found a base case incremental cost per life year saved for CTC compared to DCBE of $25,420; results of the sensitivity analysis ranged from a cost per life year saved of $4,882 for CTC compared to DCBE to a situation where CTC is more costly and less effective than DCBE.

Recommendation

Computed tomography colonography (CTC) is a relatively safe procedure. CTC, double contrast barium enema (DCBE) and colonoscopy are associated with a small risk of complications.

Evidence in relation to the comparison of CTC with colonoscopy indicates that CTC is less effective. MSAC recommends that public funding for CTC as a substitute investigation for colonoscopy should not be supported.

On the basis of the strength of evidence pertaining to the effectiveness and cost-effectiveness, MSAC recommends that public funding for CTC for exclusion of colorectal neoplasia in symptomatic or high risk patients who are either ineligible for colonoscopy due to patient contraindications or where there is an inability to perform or complete a colonoscopy, should be supported.

- The Minister for Health and Ageing accepted this recommendation on 24 August 2006.

Issue date: June 2005

NHS
National Institute for Health and Clinical Excellence

Computed tomographic colonography (virtual colonoscopy)

1 Guidance

1.1 Current evidence on the safety and efficacy of computed tomographic colonography (virtual colonoscopy) appears adequate to support the use of this procedure provided that the normal arrangements are in place for consent, audit and clinical governance.

2 The procedure

2.1 Indications

2.1.1 Computed tomographic (CT) colonography is used to examine the colon and rectum to detect abnormalities such as polyps and cancer. Polyps may be adenomatous (which have the potential to become malignant) or completely benign.

2.1.2 Colorectal cancer is the second most common cancer in women and the third most common cancer in men in the UK. Symptoms include blood in the stool, change in bowel habit, abdominal pain and unexplained weight loss. In addition to its use as a diagnostic test in symptomatic patients, CT colonography may be used in asymptomatic patients with a high risk of developing colorectal cancer.

2.1.3 Conventional colonoscopy and double-contrast barium enema are the main methods currently used for examining the colon.

2.2 Outline of the procedure

2.2.1 CT colonography involves using a CT scanner to produce two- and three-dimensional images of the entire colon and rectum. CT colonography is less invasive than conventional colonoscopy.

2.2.2 CT colonography is usually performed on an empty bowel although 'faecal tagging' may be used, which eliminates the need for a cathartic bowel preparation. Faecal tagging requires the patient to ingest an iodinated contrast agent with meals approximately 48 hours before the scan. Sedation is not usually required for CT colonography. The colon is distended by insufflation with air or carbon dioxide via a small rectal tube. Antispasmodic agents and/or contrast agents may be administered intravenously before the scan. The images are manipulated and interpreted by a radiologist.

2.3 Efficacy

2.3.1 A meta-analysis of data from 14 studies with a total of 1324 patients reported the sensitivity and specificity of CT colonography for the detection of polyps, using conventional colonoscopy as the reference standard. The pooled per-patient sensitivity for polyps 10 mm or larger was 88% (95% confidence interval [CI], 84–93%), for polyps 6–9 mm it was 84% (95% CI, 80–89%), and for polyps 5 mm or smaller it was 65% (95% CI, 57–73%). The pooled per-polyp sensitivity for polyps 10 mm or larger was 81% (95% CI, 76–85%), for polyps 6–9 mm it was 62% (95% CI, 58–67%), and for polyps 5 mm or smaller it was 43% (95% CI, 39–47%). The overall specificity for the detection of polyps 10 mm or larger was 95% (95% CI, 94–97%).

2.3.2 A study involving 1233 asymptomatic adults reported that the per-patient sensitivity for polyps 10 mm or larger was 94% (95% CI, 83–99%) for CT colonography and 88% (95% CI, 75–95%) for

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conventional colonoscopy. The per-patient sensitivity for polyps 6 mm or larger was 89% (95% CI, 83–93%) for CT colonography and 92% (95% CI, 87–96%) for conventional colonoscopy. A study of 615 patients reported per-patient sensitivities of 55% (95% CI, 40–70%) for polyps 10 mm or larger and 39% (95% CI, 30–48%) for polyps 6 mm or larger. Another study of 614 patients reported that CT colonography was significantly more sensitive than barium enema but less sensitive than colonoscopy. A study of 203 patients that used faecal tagging reported an overall per-patient sensitivity of 90% (95% CI, 86–94%). For more details, refer to the Sources of evidence (see below).

2.3.3 The Specialist Advisors noted that the procedure may fail to detect small or flat lesions, but commented that this was also the case with other diagnostic techniques.

2.4 Safety

2.4.1 No significant complications were reported in the studies. Two studies reported on the level of discomfort felt by patients during the procedure. One study reported that 1% (9/696) of patients experienced 'extreme' or 'severe' discomfort during CT colonography, compared with 4% (25/696) for colonoscopy. In the same study, less than 1% (4/617) of patients had 'extreme' or 'severe' discomfort during CT colonography compared with 29% (181/617) during a barium enema ($p < 0.001$). A second study reported that 54% (546/1005) of patients found CT colonography to be more uncomfortable than conventional colonoscopy, but this may have been affected by the fact that patients were sedated for the conventional colonoscopy but not for the CT colonography. In the same study, CT colonography was reported to be more acceptable in terms of convenience than conventional colonoscopy in 68% (686/1005) of patients.

2.4.2 In one study, 72% (357/494) of patients were reported to prefer CT colonography to conventional colonoscopy, and 97% (518/534) preferred CT colonography to double-contrast barium enema. For more details, refer to the Sources of evidence.

2.4.3 The Specialist Advisors noted that the potential complications are similar to those associated with other techniques, and include bowel perforation and reaction to the intravenous contrast medium.

2.5 Other comments

2.5.1 It was noted that this is a rapidly evolving technology, dependent on the type of equipment used and the training and experience of the operator.

2.5.2 It was noted that patient selection was important; this is an alternative procedure to barium enema, and is particularly useful in frail and elderly patients as a diagnostic tool to detect tumours.

Andrew Dillon
Chief Executive
June 2005

Information for the public

NICE has produced information describing its guidance on this procedure for patients, carers and those with a wider interest in healthcare. It explains the nature of the procedure and the decision made, and has been written with patient consent in mind. This information is available from www.nice.org.uk/IPG129publicinfo

Sources of evidence

The evidence considered by the Interventional Procedures Advisory Committee is described in the following document.

Interventional procedure overview of computed tomographic colonography (virtual colonoscopy), August 2004

Available from www.nice.org.uk/ip208overview

Ordering information
Copies of this guidance can be obtained from the NHS Response Line by telephoning 0870 1555 455 and quoting reference number N0880. *Information for the public* can be obtained by quoting reference number N0881.

The distribution list for this guidance is available at www.nice.org.uk/IPG129distributionlist

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5. Guidelines, Coverage Policies, and Policy Statements

Medicare (2007)

Aetna (2007)

USPSTF (2002)

National Cancer Institute (2007)

American Gastroenterological Association (2007)

American College of Radiology

American Society for Gastrointestinal Endoscopy (2006)

NCD for Colorectal Cancer Screening Tests (210.3)

Publication Number

100-3

Manual Section Number

210.3

Version Number

1

Effective Date of this Version

1/1/2004

Implementation Date

1/5/2004

Benefit Category

Colorectal Cancer Screening Tests

Note: This may not be an exhaustive list of all applicable Medicare benefit categories for this item or service.

Item/Service Description

FOBTs are generally divided into two types: immunoassay and guaiac types.

Immunoassay (or immunochemical) fecal occult blood tests (iFOBT) use “antibodies directed against human globin epitopes. While most iFOBTs use spatulas to collect stool samples, some use a brush to collect toilet water surrounding the stool. Most iFOBTs require laboratory processing.

Guaiac fecal occult blood tests (gFOBT) use a peroxidase reaction to indicate presence of the heme portion of hemoglobin. “Guaiac turns blue after oxidation by oxidants or peroxidases in the presence of an oxygen donor such as hydrogen peroxide. Most FOBTs use sticks to collect stool samples and may be developed in a physician’s office or a

laboratory.

Indications and Limitations of Coverage

Section 4104 of the Balanced Budget Act of 1997 provides for coverage of screening colorectal cancer procedures under Medicare Part B. Medicare currently covers: 1) annual fecal occult blood tests (FOBTs); (2) flexible sigmoidoscopy over 4 years; (3) screening colonoscopy for persons at average risk for colorectal cancer every 10 years, or for persons at high risk for colorectal cancer every 2 years; (4) barium enema every 4 years as an alternative to flexible sigmoidoscopy, or every 2 years as an alternative to colonoscopy for persons at high risk for colorectal cancer; and, (5) other procedures the Secretary finds appropriate based on consultation with appropriate experts and organizations.

Coverage of the above screening examinations was implemented in regulations through a final rule that was published on October 31, 1997 (62 FR 59079), and was effective January 1, 1998. At that time, based on consultation with appropriate experts and organizations, the definition of the term "FOBT" was defined in 42 CFR §410.37(a)(2) of the regulation to mean a “guaiac-based test for peroxidase activity, testing two samples from each of three consecutive stools.

In the 2003 Physician Fee Schedule Final Rule (67 FR 79966) effective March 1, 2003, CMS amended the FOBT screening test regulation definition at 42 CFR §410.37(a)(2) to provide that it could include either: (1) a guaiac-based FOBT, or, (2) other tests determined by the Secretary through a national coverage determination.

A. Covered Indications

Fecal Occult Blood Tests (FOBT) (effective for services performed on or after January 1, 2004)

1. History

   In 1998, Medicare began reimbursement for guaiac FOBTs, but not immunoassay type tests for colorectal cancer screening. Since the fundamental process is similar for other iFOBTs, CMS evaluated colorectal cancer screening using immunoassay FOBTs in general.
2. Expanded Coverage

Medicare covers one screening FOBT per annum for the early detection of colorectal cancer. This means that Medicare will cover one guaiac-based (gFOBT) or one immunoassay-based (iFOBT) at a frequency of every 12 months; i.e., at least 11 months have passed following the month in which the last covered screening FOBT was performed, for beneficiaries aged 50 years and older. The beneficiary completes the existing gFOBT by taking samples from two different sites of three consecutive stools; the beneficiary completes the iFOBT by taking the appropriate number of stool samples according to the specific manufacturer's instructions. This screening requires a written order from the beneficiary's attending physician. ("Attending physician means a doctor of medicine or osteopathy (as defined in §1861(r)(1) of the Social Security Act) who is fully knowledgeable about the beneficiary's medical condition, and who would be responsible for using the results of any examination performed in the overall management of the beneficiary's specific medical problem.)

B. Noncovered Indications

All other indications for colorectal cancer screening not otherwise specified above remain noncovered.

(This NCD last reviewed December 2003.)

Cross Reference

Also see NCD for Fecal Occult Blood Test (§190.34).

Transmittal Number

5

Transmittal Link

http://www.cms.hhs.gov/transmittals/downloads/R5NCD.pdf

Revision History

12/2003 - Expanded Medicare coverage for screening for early detection of colorectal cancer by adding additional fecal occult blood test (iFOBT, immunoassay-based) that can be used as alternative to existing gFOBT, guaiac-based test. Medicare coverage continues to

allow one FOBT per year for beneficiaries aged 50 and over. Effective date 1/01/04. Implementation date 1/05/2004 for coverage & HCPCS codes and 4/05/2004 for frequency edits. (TN 5) (CR 2996)

Claims Processing Instructions

- TN 3 (Medicare Benefit Policy)
- TN 52 (Medicare Claims Processing)

National Coverage Analyses (NCAs)

This NCD has been or is currently being reviewed under the National Coverage Determination process. The following are existing associations with NCAs, from the National Coverage Analyses database.

- Original consideration for Screening Immunoassay Fecal-Occult Blood Test (CAG-00180N)

Coding Analyses for Labs (CALs)

This NCD has been or is currently being reviewed under the National Coverage Determination process. The following are existing associations with CALs, from the Coding Analyses for Labs database.

- Original consideration for Prothrombin Time and Fecal Occult Blood (Revision of ICD-9-CM Codes for Injury to Gastrointestinal Tract) (CAG-00187N)

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Clinical Policy Bulletin:
Virtual Colonoscopy

Number: 0535

Policy

1. Aetna considers virtual colonoscopy using computed tomography (also known as three-dimensional computed tomographic (CT) colography, CT colonography) medically necessary for colonic evaluation of symptomatic members with a known colonic obstruction or members with an incomplete colonoscopy due to obstructive or stenosing colonic lesions; or for members who are receiving chronic anticoagulation that cannot be interrupted.

   Aetna considers virtual colonoscopy using CT experimental and investigational for all other indications, including the screening or diagnosis of colorectal cancer or inflammatory bowel disease in persons without an obstruction or incomplete colonoscopy.

2. Aetna considers virtual colonoscopy using magnetic resonance imaging (MRI) (also known as MRI colonography) experimental and investigational for the screening or diagnosis of colorectal cancer, inflammatory bowel disease, or other indications because its value for these indications has not been established.

Background

Three-dimensional computed tomographic (CT) colography, or "virtual colonoscopy," is a promising new imaging method. The technique combines the use of rapid helical CT with computer software capable of rendering images of the whole colon. Using a conventional workstation and a dynamic display of images, a radiologist conducts virtual examinations of the bowel, simulating the way endoscopists view the colon. This method is being promoted by some as a noninvasive screening test for colorectal neoplasia.

More clinical trials need to be conducted to assess the cost-effectiveness and efficacy of virtual colonoscopy in comparison with conventional colonoscopy and sigmoidoscopy.

The current cost of virtual colonoscopy probably prohibits its use as a screening tool. A major component of the cost is the time now required for a radiologist to perform the procedure. To be economically feasible for use as a screening method, the cost probably would need to drop below the cost of conventional colonoscopy, since virtual colonoscopy is only a screening test. An appreciable number of patients undergoing

virtual colonoscopy screening would need a subsequent colonoscopy and biopsy to confirm the diagnosis and to resect polyps. The need for a follow up colonoscopy must be included in any cost-effectiveness analysis of screening with virtual colonoscopy. The relatively low specificity of virtual colonoscopy in most series (i.e., the many false positive results) reduces its cost-effectiveness, because falsely positive results lead to many unnecessary follow-up conventional colonoscopies.

Scholmerich (2003) stated that virtual colonoscopy using CT or MRI does not appear to offer much help in the diagnosis of inflammatory bowel disease (Crohn's disease).

In a review, Blomqvist (2003) stated that both CT and MRI have been improved with significant advances of the technological hardware and software. This has contributed to high patient acceptance due to shorter examination times and more open configuration of the systems, consistent high quality images with better delineation of the normal abdomino-pelvic anatomy and pathology. New techniques such as CT-colonography have emerged from a research application to a clinical tool that can be used in different clinical settings. Phased-array receiver coils have significantly increased the usefulness of MRI in the evaluation of rectal neoplasms due to the high resolution that can be obtained. New organ specific contrast agents for magnetic resonance imaging have facilitated the preoperative evaluation of liver metastases in favor of more invasive techniques with similar sensitivities. However, preoperative staging criteria for colorectal cancer using CT and MRI have to be updated and the results of new techniques have to be confirmed in large clinical trials. In the future, further development of CT and MRI may offer "one-stop shopping" protocols for both diagnosis, local and distant staging of colorectal cancer.

Pickhardt et al (2003) reported that CT virtual colonoscopy with the use of a 3-D approach is an accurate screening method for the detection of colorectal neoplasia in asymptomatic average-risk adults and compares favorably with optical colonoscopy in terms of the detection of clinically relevant lesions. However, in an editorial that accompanied the study by Pickhardt et al, Morrin and LaMont (2003) stated that "if the results of this well-designed study are reproducible on a wider scale, and if the important questions regarding the appropriate size threshold and surveillance of smaller polyps can be resolved, then screening virtual colonoscopy is ready for prime time".

A study by Cotton, et al. (2004) reported that the accuracy of CT colonography (virtual colonoscopy) for the detection of colorectal cancer is less reliable than previously thought. CT colonography involves the examination of computer-generated images of the colon constructed from data obtained from an abdominal computed tomographic examination. Several studies have suggested a high degree of sensitivity for CT colonography; however, those results were obtained at single, specialized centers. Cotton reported on a new study that was designed to evaluate the accuracy of CT colonography in routine practice at nine major hospital centers.

In this study, researchers assessed the accuracy of CT colonography in 615 patients aged 50 years or older who were referred for routine, clinically indicated colonoscopy

(Cotton, et al., 2004). Colonoscopy was performed within 2 hours of the colonography and results were compared. The sensitivity of CT colonography for detecting one or more lesions sized at least 6 mm was 39% and for lesions sized at least 10 mm, it was 55%. These results were significantly lower than those for conventional colonoscopy, with sensitivities of 99% and 100%, respectively. CT colonography missed two of eight cancers. The accuracy of CT colonography varied considerably between centers. At the one center that had "substantial" prior experience with CT colonography, the sensitivity was 82% for lesions of 6 mm or more. Sensitivity at all of the other centers combined was 24%, with no improvement in accuracy as the number of cases at each center was increased. Preference questionnaires after both procedures were performed showed that 46% of the patients preferred CT colonography versus 41% who preferred conventional colonoscopy.

The authors stated that "even if the results of CT colonography continue to be good in the hands of experts, it has yet to be proven that this expertise can be taught and disseminated reliably into daily practice". The authors concluded that CT colonography is not yet ready for widespread clinical application; techniques and training need to be improved. This is in agreement with the update of the clinical guidelines on colorectal cancer screening and surveillance that were prepared by a panel convened by the U.S. Agency for Health Care Policy and Research and published in 1997 under the sponsorship of a consortium of gastroenterology societies (Winawer et al, 2003). It stated that promising new screening tests (virtual colonoscopy and tests for altered DNA in stool) are in development but are not yet ready for use outside of research studies. In addition, the American College of Gastroenterology does not recommend virtual colonoscopy for screening colorectal cancers. It states that more research is needed to verify the validity and generalizeability of the 3-D approach to polyp detection. It will also be necessary to develop recommendations for training in CT colonography as well as requirements of hardware and software systems and specification of methods for technical performance. Systems that allow same-day polypectomy on patients with positive CT colonography studies are not yet widely available (Rex, 2004)

A technology assessment by the BlueCross BlueShield Association Technology Evaluation Center (2004) concluded that CT colonography does not meet the TEC criteria because the available evidence is insufficient to reach conclusions about the effect CT colonography on health outcomes.

An assessment prepared for the Ontario Ministry of Health and Long-Term Care (2003) found that, "[a]lthough [CT colonography] offers the potential advantage of being less invasive than colonoscopy and has the ability to image the entire colon, it lacks the necessary sensitivity required for screening." The assessment noted that, in addition, unlike standard colonoscopy, CT colonography (CTC) "offers no therapy that can be applied once an abnormality is detected"; standard colonoscopy is necessary to resect lesions detected by CT colonography. The assessment concluded that "[w]ith the limited sensitivity and specificity of CTC relative to colonoscopy, together with the lack of therapeutic intervention, this method of screening may result in inconvenience, cost, and complications of both tests" and that "[b]ased on the current evidence, CTC cannot

be proposed for population-based colorectal cancer screening." The assessment explained that "[p]atients with colonic symptoms or a personal/family history of polyps will benefit more in several ways if they undergo colonoscopy including excision of premalignant polyps."

The assessment concluded, however, that CT colonography can be considered for diagnostic purposes in patients in whom performing colonoscopy is clinically contraindicated or for those patients who had incomplete colonoscopy because of stenosis or obstruction of the colon (Ontario Ministry of Health and Long-Term Care, 2003). In support of this conclusion, the assessment reasoned that that CT colonography is able to visualize the entire colon in most patients with occlusive tumors or stenosing lesions, and that CT colonography may be preferable to barium enema in terms of the extent of the proximal colon that can be visualized and in terms of detecting extracolonic lesions.

An American Gastroenterological Association (AGA) Task Force Report (Van Dam, et al., 2004) concluded that, although virtual colonoscopy has significant promise, the technology is still evolving and results of virtual colonoscopy for screening are highly variable.

According to the University of Michigan Health System's guidelines on adult preventive health care (2004), recommended methods for colon cancer screening include fecal occult-blood testing, flexible sigmoidoscopy or colonoscopy. Winawer (2005) noted that "several options are now available for screening of colorectal cancer, and the emerging technology of stool DNA testing and virtual colonoscopy shows promise …There are quality-control issues at every step." van Gelder et al (2005) stated that "despite a growing body of evidence, it remains uncertain to what extent patient acceptance, radiation issues, flat lesions, and extracolonic findings will be a stumbling block to using CT colonography for colorectal cancer screening."

An assessment by the Danish Centre for Health Technology Assessment (DACEHTA, 2005) concluded that "[d]espite the potential economic benefits, CT colonography should not replace colonoscopy as the primary diagnostic method in a Danish outpatient colonoscopy population. Such a strategy requires further research at a few centres before widespread use in routine clinical practice."

In a meta-analysis on CT colonography, Mulhall et al (2005) concluded that "computed tomographic colonography is highly specific, but the range of reported sensitivities is wide. Patient or scanner characteristics do not fully account for this variability, but collimation, type of scanner, and mode of imaging explain some of the discrepancy. This heterogeneity raises concerns about consistency of performance and about technical variability. These issues must be resolved before CT colonography can be advocated for generalized screening for colorectal cancer". In an editorial that accompanied the article by Mulhall et al, Imperiale (2005) stated that "until we understand more about the factors – both within and among institutions – that are responsible for the varying sensitivity of CT colonography, we should not recommend it

as a screening test."

An assessment prepared for the Swedish Council on Health Technology Assessment (SBU, 2004) summarized current evidence for CT colonography: "Most studies have shown that CT colonography offers high diagnostic reliability for malignant tumors and polyps 10 mm or larger, inconsistent diagnostic reliability for changes of 5 to 9 mm, and insufficient diagnostic reliability for changes smaller than 5 mm. Some studies, however, have shown unacceptable diagnostic reliability even for malignant tumors and polyps larger than 10 mm." The assessment stated that CT colonography may compare favorably to barium enema. The assessment explained: "The extent to which CT colonography can replace double-contrast barium enema in patients with disease symptoms has not been completely studied since CT colonography almost exclusively has been compared to colonoscopy. However, the diagnostic reliability of CT colonography compared to colonoscopy appears to be at least equal to the diagnostic reliability of double contrast barium enema compared to colonoscopy." The assessment explained that one advantage of CT colonography is that, in findings of colon tumors, CT colonography can, in the same examination, also provide information on changes in adjacent tissues and metastases in the lymph nodes and liver. The assessment stated that another advantage of CT colonography is that patients usually experience less discomfort and pain with CT colonography than with conventional colonoscopy and double-contrast barium enema. The assessment noted, however, that it generally is not the examination per se that causes the most discomfort for the patient, but the pre-examination procedure, i.e., the use of laxatives, that is similar in all of the methods of examining the colon.

On the other hand, the National Institute for Health and Clinical Excellence (2005) stated that "Current evidence on the safety and efficacy of computed tomographic colonoscopy (virtual colonoscopy) appears adequate to support the use of this procedure provided that the normal arrangements are in place for consent, audit and clinical governance."

Guidelines on evaluation of patients with lower gastrointestinal bleeding from the American Society for Gastrointestinal Endoscopy (2005) state that "[v]irtual colonoscopy or computed tomographic (CT) colonography also can be used to rule out a proximal colonic lesion in patients who have had an incomplete colonoscopy."

Virtual colonoscopies should only be performed at centers with an appropriate generation of CT scan – a minimum 4 detector CT scanner; collimation of 3 mm or less, overlapping sections at an interval that is two-thirds or less of the collimation, and scan times should be 30 seconds or less in order to minimize respiratory motion.

CPT Codes / HCPCS Codes / ICD-9 Codes

CPT codes covered if selection criteria are met:

0067T

CPT codes not covered for indications listed in the CPB:

0066T

Other CPT codes related to the CPB:

45378 - 45392
with 53
modifier

72192 - 72194

72195 - 72197

74150 - 74170

74181 - 74183

Other HCPCS codes related to the CPB:

G0105	Colorectal cancer screening; colonoscopy on individual at high risk
G0106	Colorectal cancer screening; alternative to G0104, screening sigmoidoscopy, barium enema
G0120	Colorectal cancer screening; alternative to G0105, screening colonoscopy, barium enema
G0121	Colorectal cancer screening; colonoscopy on individual not meeting criteria for high risk
G0122	Colorectal cancer screening; barium enema

ICD-9 codes covered if selection criteria are met:

560.81	Intestinal or peritoneal adhesions with obstructions with obstruction (postoperative) (postinfection)
560.89	Other specified intestinal obstruction
560.9	Unspecified intestinal obstruction
751.2	Atresia and stenosis of large intestine, rectum, and anal canal
V58.61	Long-term use of anticoagulants [that cannot be interrupted]

Other ICD-9 codes related to the CPB:

153.0 - 153.9	Malignant neoplasm of colon
154.0	Malignant neoplasm of rectosigmoid junction
197.5	Secondary malignant neoplasm of large intestine and rectum
211.3	Benign neoplasm of colon
211.4	Benign neoplasm of rectum and anal canal
230.3	Carcinoma in situ of colon

230.4	Carcinoma in situ of rectum
230.5	Carcinoma in situ of anal canal
230.6	Carcinoma in situ of anus, unspecified
235.2	Neoplasm of uncertain behavior of stomach, intestines, and rectum
555.1	Regional enteritis of large intestine
556.0 - 556.9	Ulcerative colitis
558.1 - 558.9	Other and unspecified non-infectious gastroenteritis and colitis
562.10	Diverticulosis of colon (without mention of hemorrhage)
562.11	Diverticulitis of colon without mention of hemorrhage
562.12	Diverticulosis of colon with hemorrhage
562.13	Diverticulitis of colon with hemorrhage
564.1	Irritable bowel syndrome
564.7	Megacolon, other than Hirschsprung's
569.0	Anal and rectal polyp
569.1	Rectal prolapse
569.3	Hemorrhage of rectum and anus
V76.51	Special screening for malignant neoplasm of colon

The above policy is based on the following references:

1. Bond JH. Screening guidelines for colorectal cancer. Am J Med. 1999;106:Suppl 1A:7S-10S.
2. Fenlon HM, Nunes DP, Schroy PC III, et al. A comparison of virtual and conventional colonoscopy for the detection of colorectal polyps. N Engl J Med. 1999;341:1496-1503.
3. Rex DK, Vining D, Kopecky KK. An initial experience with screening for colon polyps using spiral CT with and without CT colography. Gastrointest Endosc. 1999;50:309-313.
4. Akerkar GA, Yee J , Hung R , et al. Patient experience and preferences toward colon cancer screening: A comparison of virtual colonoscopy and conventional colonoscopy. Gastrointest Endosc. 2001;54(3):310-315.
5. Rex DK, Cutler CS, Lemmel GT, et al. Colonoscopic miss rates of adenomas determined by back-to-back colonoscopies. Gastroenterology. 1997;112(1):24-28.
6. Winawer SJ, Fletcher RH, Miller L, et al. Colorectal cancer screening: Clinical guidelines and rationale. Gastroenterology. 1997;112:594-642.
7. Byers T, Levin B, Rothenberger D, et al. American Cancer Society guidelines for screening and surveillance for early detection of colorectal polyps and cancer: Update 1997. CA Cancer J Clin. 1997;47:154-160.

8. Hara AK, Johnson CD, Reed JE, et al. Detection of colorectal polyps with CT colography: Initial assessment of sensitivity and specificity. Radiology. 1997;205:59-65.
9. Rex DK, Lehman GA, Ulbright TM, et al. Colonic neoplasia in asymptomatic persons with negative fecal occult blood tests: Influence of age, gender, and family history. Am J Gastroenterol. 1993;88:825-831.
10. Rogge JD, Elmore MF, Mahoney SJ, et al. Low-cost, office-based, screening colonoscopy. Am J Gastroenterol. 1994;89:1775-1780.
11. Hixson LJ, Fennerty MB, Sampliner RE, et al. Prospective blinded trial of the colonoscopic miss-rate of large colorectal polyps. Gastrointest Endosc. 1991;37:125-127.
12. Schrock TR. Colonoscopy versus barium enema in the diagnosis of colorectal cancer and polyps. Gastrointest Endosc Clin North Am. 1993;3:585-610.
13. Bond JH. Colorectal cancer screening: The potential role of virtual colonoscopy. J Gastroenterol. 2002;37 Suppl 13:92-96.
14. Gluecker TM, Fletcher JG. CT colonography (virtual colonoscopy) for the detection of colorectal polyps and neoplasms. Current status and future developments. Eur J Cancer. 2002;38(16):2070-2078.
15. Rex DK. Considering virtual colonoscopy. Rev Gastroenterol Disord. 2002;2(3):97-105.
16. Pijl ME, Chaoui AS, Wahl RL, et al. Radiology of colorectal cancer. Eur J Cancer. 2002;38(7):887-898.
17. Mendelson RM, Forbes GM. Computed tomography colonography (virtual colonoscopy): Review. Australas Radiol. 2002;46(1):1-12.
18. Scholmerich J. Inflammatory bowel disease. Endoscopy. 2003;35(2):164-170.
19. Blomqvist L. Preoperative staging of colorectal cancer--computed tomography and magnetic resonance imaging. Scand J Surg. 2003;92(1):35-43.
20. L'Agence Nationale d'Accreditation d'Evaluation en Sante (ANAES). Virtual colonoscopy [summary]. Paris, France: ANAES; 2000.
21. Institute for Clinical Systems Improvement (ICSI). Computed tomographic colonography for detection of colorectal polyps and neoplasms. Technology Assessment Report. Bloomington, MN: ICSI; 2001.
22. State of Minnesota, Health Technology Advisory Committee (HTAC). Computed tomographic colonography (virtual colonoscopy). St. Paul, MN: HTAC; 2002.
23. Canadian Coordinating Office for Health Technology Assessment (CCOHTA). Virtual colonoscopy (computed tomography colonography). Ottawa, ON: CCOHTA; 2002.
24. Medical Services Advisory Committee (MSAC). Virtual colonoscopy. Horizon Scanning 001. Canberra, Australia: MSAC; 2002.
25. Pickhardt PJ, Choi JR, Hwang I, et al. Computed tomographic virtual colonoscopy to screen for colorectal neoplasia in asymptomatic adults. N Engl J Med. 2003;349(23):2191-2200.
26. Morrin MM, LaMont JT. Screening virtual colonoscopy--ready for prime time? N Engl J Med. 2003;349(23):2261-2264.
27. Winawer S, Fletcher R, Rex D, et al. Colorectal cancer screening and

surveillance: Clinical guidelines and rationale-Update based on new evidence. Gastroenterology. 2003;124(2):544-560.
28. Mundy L, Merlin T. Virtual colonoscopy: Non-invasive CT scanning technique for screening patients with possible bowel disease. Horizon Scanning Prioritising Summary - Volume 2. Adelaide, Australia: Adelaide Health Technology Assessment (AHTA) on behalf of National Horizon Scanning Unit (HealthPACT and MSAC); 2003.
29. Ontario Ministry of Health and Long-Term Care, Medical Advisory Secretariat. Computed tomography colonography. Health Technology Scientific Literature Review. Toronto, ON: Ontario Ministry of Health and Long-Term Care; October 2003.
30. Institute for Clinical Systems Improvement (ICSI). Computed tomographic colonography for detection of colorectal polyps and neoplasms. Technology Assessment Report No. 58. Bloomington, MN: ICSI; October 2004.
31. Cotton PB, Durkalski VL, Pineau BC, et al. Computed tomographic colonography (virtual colonoscopy): A multicenter comparison with standard colonoscopy for detection of colorectal neoplasia. JAMA. 2004;291(14):1713-1719.
32. Rex DK; ACG Board of Trustees. American College of Gastroenterology action plan for colorectal cancer prevention. Am J Gastroenterol. 2004;99(4):574-577.
33. BlueCross BlueShield Association (BCBSA), Technology Evaluation Center (TEC). CT colonography ("virtual colonoscopy") for colon cancer screening. TEC Assessment Program. Chicago, IL: BCBSA; July 2004;19(6). Available at: http://www.bcbs.com/tec/vol19/19_06.html.. Accessed August 19, 2005.
34. Van Dam J, Cotton P, Johnson CD, et al. AGA future trends report: CT-Colonography. Gastroenterology. 2004;127(3):970-984.
35. Purkayastha S, Tekkis P P, Athanasiou T, et al. Magnetic resonance colonography versus colonoscopy as a diagnostic investigation for colorectal cancer: A meta-analysis. Clin Radiol. 2005;60(9):980-989.
36. University of Michigan Health System. Adult preventive health care: Cancer screening. Ann Arbor, MI: University of Michigan Health System; May 2004.
37. Winawer SJ. Screening of colorectal cancer: Progress and problems. Recent Results Cancer Res. 2005;166:231-244.
38. van Gelder RE, Florie J, Stoker J. Colorectal cancer screening and surveillance with CT colonography: Current controversies and obstacles. Abdom Imaging. 2005;30(1):5-12.
39. Danish Centre for Evaluation and Health Technology Assessment (DACEHTA). Colon examination with CT colonography. A health technology assessment. Summary. Danish Health Technology Assessment -- grant funded projects 2005;5(3). Copenhagen, Denmark: National Board of Health; 2005.
40. Mulhall BP, Veerappan GR, Jackson JL. Meta-analysis: Computed tomographic colonography. Ann Intern Med. 2005;142(8):635-650.
41. Imperiale TF. Can computed tomographic colonography become a 'good' screening test? Ann Intern Med. 2005;142(8):669-670.
42. Swedish Council on Technology Assessment in Health Care (SBU). CT colonography (virtual colonoscopy) -- Early assessment briefs (Alert).

Stockholm, Sweden: Swedish Council on Technology Assessment in Health Care (SBU); 2004.
43. National Institute for Health and Clinical Excellence (NICE). Computed tomographic colonoscopy (virtual colonoscopy). Interventional Procedure Guidance 129. London, UK: NICE; June 2005. Available at: http://www.nice.org.uk/page.aspx?o=262011. Accessed July 27, 2005.
44. Harford WV. Colorectal cancer screening and surveillance. Surg Oncol Clin N Am. 2006;15(1):1-20, v.
45. Mackalski BA, Bernstein CN. New diagnostic imaging tools for inflammatory bowel disease. Gut. 2006;55(5):733-741.
46. Davila RE, Rajan E, Adler DG, et al. ASGE guideline: The role of endoscopy in the patient with lower-GI bleeding. Gastrointest Endosc. 2005;62(5):656-660.
47. Heiken JP, Bree RL, Foley WD, et al; Expert Panel on Gastrointestinal Imaging. Colorectal cancer screening. American College of Radiology (ACR) Appropriateness Criteria. Reston, VA: ACR; 2006.
48. Purkayastha S, Athanasiou T, Tekkis PP, et al. Magnetic resonance colonography vs computed tomography colonography for the diagnosis of colorectal cancer: An indirect comparison. Colorectal Dis. 2007;9(2):100-111.
49. Rosman AS, Korsten MA. Meta-analysis comparing CT colonography, air contrast barium enema, and colonoscopy. Am J Med. 2007;120(3):203-210.
50. Halligan S, Taylor SA. CT colonography: Results and limitations. Eur J Radiol. 2007;61(3):400-408.

Screening for Colorectal Cancer

Recommendations and Rationale

U.S. Preventive Services Task Force

This statement summarizes the current U.S. Preventive Services Task Force (USPSTF) recommendations on screening for colorectal cancer and the supporting scientific evidence, and it updates the 1996 recommendations contained in the *Guide to Clinical Preventive Services*, second edition.[1] At that time, the USPSTF recommended screening for colorectal cancer with annual fecal occult blood testing (FOBT), periodic sigmoidoscopy, or the combination of FOBT and sigmoidoscopy but concluded that the evidence was insufficient to recommend for or against colonoscopy or barium enema. Explanations of the ratings and of the strength of overall evidence are given in Appendix A and Appendix B, respectively. The complete information on which this statement is based, including evidence tables and references, is available in the article Screening for Colorectal Cancer in Adults at Average Risk: A Summary of the Evidence for the U.S. Preventive Services Task Force[2] (which follows this recommendation) and in the Systematic Evidence Review[3] on this topic. These documents can be obtained through the USPSTF Web site (www. preventive services.ahrq.gov), and through the National Guideline Clearinghouse (www.guideline.gov). The summary of the evidence and the recommendation statement are also available in print through the AHRQ Publications Clearinghouse (call 1-800-358-9295 or e-mail ahrqpubs@ahrq.gov).

Summary of Recommendation

The USPSTF strongly recommends that clinicians screen men and women 50 years of age or older for colorectal cancer. **A recommendation.**

The USPSTF found fair to good evidence that several screening methods are effective in reducing mortality from colorectal cancer. The USPSTF concluded that the benefits from screening substantially outweigh potential harms, but the quality of evidence, magnitude of benefit, and potential harms vary with each method.

The USPSTF found good evidence that periodic fecal occult blood testing (FOBT) reduces mortality from colorectal cancer and fair evidence that sigmoidoscopy alone or in combination with FOBT reduces mortality. The USPSTF did not find direct evidence that screening colonoscopy is effective in reducing colorectal cancer mortality; efficacy of colonoscopy is supported by its integral role in trials of FOBT, extrapolation from sigmoidoscopy studies, limited case-control evidence, and the ability of colonoscopy to inspect the proximal colon. Double-contrast barium enema offers an alternative means of whole-bowel examination, but it is less sensitive than colonoscopy, and there is no direct evidence that it is effective in reducing mortality rates. The USPSTF found insufficient evidence that newer screening technologies (for example, computed tomographic colography) are effective in improving health outcomes.

There are insufficient data to determine which strategy is best in terms of the balance of benefits and potential harms or cost-effectiveness. Studies reviewed by the USPSTF indicate that colorectal cancer screening is likely to be cost-effective (less than $30,000 per additional year of life gained) regardless of the strategy chosen.

It is unclear whether the increased accuracy of colonoscopy compared with alternative screening methods (for example, the identification of lesions that

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FOBT and flexible sigmoidoscopy would not detect) offsets the procedure's additional complications, inconvenience, and costs.

Clinical Considerations

- Potential screening options for colorectal cancer include home FOBT, flexible sigmoidoscopy, the combination of home FOBT and flexible sigmoidoscopy, colonoscopy, and double-contrast barium enema. Each option has advantages and disadvantages that may vary for individual patients and practice settings. The choice of specific screening strategy should be based on patient preferences, medical contraindications, patient adherence, and available resources for testing and follow-up. Clinicians should talk to patients about the benefits and potential harms associated with each option before selecting a screening strategy.
- The optimal interval for screening depends on the test. Annual FOBT offers greater reductions in mortality rates than biennial screening but produces more false-positive results. A 10-year interval has been recommended for colonoscopy on the basis of evidence regarding the natural history of adenomatous polyps. Shorter intervals (5 years) have been recommended for flexible sigmoidoscopy and double-contrast barium enema because of their lower sensitivity, but there is no direct evidence with which to determine the optimal interval for tests other than FOBT. Case-control studies have suggested that sigmoidoscopy every 10 years may be as effective as sigmoidoscopy performed at shorter intervals.
- The USPSTF recommends initiating screening at 50 years of age for men and women at average risk for colorectal cancer, based on the incidence of cancer above this age in the general population. In persons at higher risk (for example, those with a first-degree relative who receives a diagnosis with colorectal cancer before 60 years of age), initiating screening at an earlier age is reasonable.
- Expert guidelines exist for screening very high-risk patients, including those with a history suggestive of familial polyposis or hereditary nonpolyposis colorectal cancer, or those with a personal history of ulcerative colitis.[4] Early screening with colonoscopy may be appropriate, and genetic counseling or testing may be indicated for patients with genetic syndromes.
- The appropriate age at which colorectal cancer screening should be discontinued is not known. Screening studies have generally been restricted to patients younger than 80 years of age, with colorectal cancer mortality rates beginning to decrease within 5 years of initiating screening. Yield of screening should increase in older persons (because of higher incidence of colorectal cancer), but benefits may be limited as a result of competing causes of death. Discontinuing screening is therefore reasonable in patients whose age or comorbid conditions limit life expectancy.
- Proven methods of FOBT screening use guaiac-based test cards prepared at home by patients from three consecutive stool samples and forwarded to the clinician. Whether patients need to restrict their diet and avoid certain medications is not established. Rehydration of the specimens before testing increases the sensitivity of FOBT but substantially increases the number of false-positive test results. Neither digital rectal examination (DRE) nor the testing of a single stool specimen obtained during DRE is recommended as an adequate screening strategy for colorectal cancer.
- The combination of FOBT and sigmoidoscopy may detect more cancers and more large polyps than either test alone, but the additional benefits and potential harms of combining the two tests are uncertain. In general, FOBT should precede sigmoidoscopy because a positive test result is an indication for colonoscopy, obviating the need for sigmoidoscopy.
- Colonoscopy is the most sensitive and specific test for detecting cancer and large polyps but is associated with higher risks than other screening tests for colorectal cancer. These include a small risk for bleeding and risk for perforation, primarily associated with removal of polyps or

biopsies performed during screening. Colonoscopy also usually requires more highly trained personnel, overnight bowel preparation, sedation, and longer recovery time, which may necessitate transportation for the patient. It is not certain whether the potential added benefits of colonoscopy relative to screening alternatives are large enough to justify the added risks and inconvenience for all patients.

- Initial costs of colonoscopy are higher than the costs of other tests. Estimates of cost-effectiveness, however, suggest that, from a societal perspective, compared with no screening, all methods of colorectal cancer screening are likely to be as cost-effective as many other clinical preventive services—less than $30,000 per additional year of life gained.

Scientific Evidence

Epidemiology and Clinical Consequences

Colorectal cancer is the fourth most common cancer in the United States and the second leading cause of cancer death. A person at age 50 has about a 5% lifetime risk of being diagnosed with colorectal cancer and a 2.5% chance of dying from it[4]; the average patient dying of colorectal cancer loses 13 years of life.[5]

More than 80% of colorectal cancers arise from adenomatous polyps. Although fewer than 1% of adenomatous polyps less than 1 cm will eventually develop into cancer, 10% of adenomatous polyps greater than 1 cm become malignant within 10 years, and about 25% become malignant after 20 years.[6] The prevalence of adenomatous polyps increases from 20% to 25% at age 50 to 50% by age 75-80.[7]

Most colorectal cancers occur in persons at average risk, but 20% occur among patients with specific risk factors, such as those with a family history of colorectal cancer in a first-degree relative. A small proportion (6%) is associated with uncommon genetic syndromes such as familial adenomatous polyposis [FAP] or hereditary nonpolyposis colorectal cancer [HNPCC]. Other persons at increased risk include patients with longstanding ulcerative colitis, persons with previously diagnosed large adenomatous polyps or colorectal cancer, and those with a family history of adenomatous polyps diagnosed before age 60.

Accuracy and Reliability of Screening Tests

The USPSTF reviewed evidence of the effectiveness of the following screening tests for colorectal cancer: DRE, FOBT, sigmoidoscopy, colonoscopy, DCBE, and CT colography, singly and in various combinations.

Digital Rectal Examination/Office FOBT

There is little evidence to determine the effectiveness of either DRE or a single office FOBT using a stool sample obtained on DRE. Fewer than 10% of colorectal cancers arise within reach of the examining finger, and some of these lesions will already be symptomatic. The sensitivity of a single office FOBT is likely to be substantially lower than that of screening protocols involving multiple test cards: in 1 study the first test card would have missed 42% of cancers detected by screening.[8] Samples collected by DRE may be affected by other limitations, including inadequate amount of stool or trauma from the exam.

Fecal Occult Blood Testing

Sensitivity of FOBT screening varies with the testing protocol. Sensitivity and specificity of a single test have been estimated at 40% and 96% to 98%, respectively. Hydration of specimen increases sensitivity (60%) but reduces specificity (90%).[9] Of patients who have a positive FOBT using rehydrated slides, only 2% will have cancer; 6% to 8% will have cancer or a large polyp. Using unrehydrated specimens, 5% to 18% of patients with a positive test will have cancer; 20% to 40% will have large polyps or cancer. The probability of cancer increases as the number of positive test windows increase. Tests that incorporate quantitative measures of heme and genetic stool markers have not been evaluated with respect to mortality reduction. Sensitivity and

specificity change when screening is analyzed as a program of periodic screens. Annual screening with hydrated specimens detected 49% of all incident cancers, but 38% of all subjects had at least 1 colonoscopy due to positive results.[10] Programs using unrehydrated specimens and/or biennial testing detect a smaller proportion of cancers (27% to 39%) but require fewer colonoscopies (5% to 28%).[11,12]

Sigmoidoscopy

First-time sigmoidoscopic screening detects approximately 7 cancers and about 60 large or high-risk polyps per 1,000 examinations.[13] Although sigmoidoscopy can only visualize the lower half of the colon,[14] it has been estimated to identify 80% of all patients with significant findings in the colon, because findings on sigmoidoscopy will trigger examination of the entire colon. It is difficult to quantify the "false-positive" rate of endoscopic screening, but screening may lead to the removal of many polyps that are of low malignant potential or that would not have caused clinical disease.

FOBT and Sigmoidoscopy

Combining FOBT and periodic sigmoidoscopy has been advocated to improve the sensitivity of screening. In 3 recent randomized trials, performing flexible sigmoidoscopy in addition to FOBT yielded approximately 7 additional cancers or large polyps per 1,000 patients compared to FOBT alone.[3] Adding FOBT did not improve the yield over sigmoidoscopy alone at the initial screening in these studies, which used flexible sigmoidoscopy, but did in an earlier study that used rigid sigmoidoscopy. Whether additional rounds of FOBT screening will have added benefits over flexible sigmoidoscopy has not been assessed.

Double Contrast Barium Enema

Most studies of DCBE have important limitations for determining accuracy in an asymptomatic screening population. Previous studies have reported high sensitivity (86% to 90%) of DCBE for colorectal cancer and polyps, and high specificity (95%). In the National Polyp Study, however, DCBE detected only 48% of polyps greater than 1 cm.[15] Sensitivity might be higher in a typical screening population where the proportion of large polyps is higher. Specificity of DCBE in this study was 85%.

Colonoscopy

Colonoscopy recently has been advocated for screening, usually at 10-year intervals or as a once-in-a-lifetime examination at age 55-65. The accuracy of colonoscopy is difficult to evaluate because it is usually considered the criterion standard. Estimated sensitivity of a single exam is 90% for large polyps and 75% for small polyps (less than 1 cm).[16] As with sigmoidoscopy, specificity is difficult to define. Many patients will have polyps detected or removed on colonoscopy, but only a minority of those would have developed cancer.

Computed Tomography (CT) Colography

CT colography, or "virtual colonoscopy," is a noninvasive procedure for producing images of the colonic lumen. The examination, which can be performed in 10 to 15 minutes, currently requires a preparation similar to colonoscopy, followed by installation of air through a rectal tube. Although CT colography can be relatively sensitive and specific in research settings (85% to 90%), recent reports have suggested lower accuracy when performed by less experienced examiners. Small and flat polyps are less well visualized on CT colography than are cancers and large polyps. Studies have not yet examined clinical outcomes with CT colography screening.

Effectiveness of Early Detection

Fecal Occult Blood Testing

Three randomized controlled trials (RCTs), all using the Hemoccult® test kit, show reductions in risk of death from colorectal cancer from 15% to 33% from periodic FOBT screening. Two European trials, which randomized patients prior to agreement to participate and used biennial screening and unrehydrated test cards, found 15% to 18%

reductions in mortality.[11,12] In a U.S. study, which randomized volunteers and used rehydrated test cards, colorectal cancer mortality after 18 years of follow-up was 33% lower among persons advised to undergo annual FOBT than among controls who received usual care (9.46 versus 14.09 deaths per 1,000 patients screened); biennial screening reduced mortality by 21%.[10,17] A fourth trial conducted in Sweden has not reported final mortality results, but no significant mortality reduction was reported after 2 rounds of rehydrated testing (RR, 0.88; 95% CI, 0.69 to 1.12).

Sigmoidoscopy

Current evidence of the effectiveness of sigmoidoscopy is limited to several well-designed case-control studies, but 2 ongoing RCTs of screening with flexible sigmoidoscopy are expected to report results within 5 years. A case-control study in a large health plan that had implemented rigid sigmoidoscopy screening suggested that screening reduced the risk of death from cancers within reach of the rigid sigmoidoscope by 59%.[18] A second case-control study in which 75% of the examinations were performed with a flexible instrument found similar protection.[19]

FOBT and Sigmoidoscopy

No RCTs have examined whether combining FOBT and sigmoidoscopy would lower mortality or morbidity more than either test alone. In a nonrandomized, controlled study involving more than 12,000 first-time attendees at a preventive-health clinic screened using rigid sigmoidoscopy, the addition of FOBT detected more cancers on initial screening than sigmoidoscopy alone, but mortality after 9 years was not significantly lower (0.36 per 1,000 patient-years in patients receiving both tests versus 0.63 per 1,000 patient years in controls; P = 0.11).[20] Whether results are generalizable to flexible sigmoidoscopy is uncertain.

Double Contrast Barium Enema

No trial has examined the ability of screening barium enema to reduce the incidence or mortality from colorectal cancer.

Colonoscopy

The effectiveness of colonoscopy to prevent colorectal cancer or mortality has not been tested in a randomized clinical trial. The National Polyp Study, a randomized trial of different intervals of surveillance after polypectomy, estimated that 76% to 90% of cancers could be prevented by regular colonoscopic surveillance exams.[21] These results should be interpreted with caution, however, because they are based on historical controls, and trial participants had more complete polyp removal than may occur in the screening setting. A single case-control study suggests that colonoscopy is associated with lower incidence of colon cancer (odds ratio [OR], 0.47; 95% CI, 0.37 to 0.58) and lower mortality from colorectal cancer (OR, 0.43;95% CI, 0.30 to 0.63).[22] Slightly greater benefits of colonoscopy have been predicted in models that project benefits based on sensitivity of screening and rates of polyp progression.

CT colography

No studies have evaluated the effectiveness of CT colography in reducing morbidity or mortality from colorectal cancer.

When to Start or Stop Screening for Colorectal Cancer

There are few data to determine optimal age for starting or stopping screening. FOBT has been proven effective for persons aged 50-80 and sigmoidoscopy is associated with reduced mortality in persons older than 45. One cost-effectiveness model suggests that beginning screening at age 40 rather than at age 50 would offer less than a 1-day average improvement in life expectancy. Randomized trials suggest that a life expectancy of at least 5 years may be required to realize the benefits of screening.

Potential Harms of Screening

FOBT has few potential harms but false-positive tests can lead to invasive procedures such as colonoscopy. Sigmoidoscopy can, in rare instances, lead to bowel perforation (1 to 2 per 10,000 examinations).[23] In a study of 1,235 screening sigmoidoscopies, adverse effects included pain

(14%), anxiety, bleeding (3%), gas or flatus (25%), but no perforations.[13] One patient died from complications after surgery to remove a severely dysplastic adenoma. A survey of barium enema experience reported that important complications of any type occurred in 1 in 10,000 examinations; perforation occurred in 1 in 25,000 examinations; death in 1 in 55,000 examinations.[24]

Screening colonoscopy poses higher risks than FOBT or sigmoidoscopy, both because it is a more invasive procedure and because generally it is used with conscious sedation, which may lead to complications. The risks of colonsocopy depend on whether it is used simply for screening and diagnosis, or whether it is also used for therapeutic procedures (eg, removal of polyps). In 2 studies of screening colonoscopies in more than 5,000 patients, 0.2% to 0.3% had major complications during or immediately after the procedures, the most common being bleeding requiring hospitalization or emergency care.[25,26]

Risks are higher in therapeutic procedures (eg, when polypectomy is performed) than in diagnostic or screening procedures. Rates of perforation for diagnostic procedures in 16 published studies ranged from 0.03% to 0.61%. There are few data on bleeding complications, but 1 study reported no bleeding events in 250 patients.[3]

The complication rates for therapeutic procedures were higher in some studies: 0.07% to 0.72% for perforations and 0.2% to 2.67% for bleeding. Death was rare (between 1 in 16,000 to 1 in 27,000) and more likely in symptomatic patients with acute problems or those with comorbid conditions. The mortality rate as a result of screening is likely to be on the lower end of this range. Complication rates could increase, however, if widespread adoption of colonoscopy leads to more procedures by less skilled endoscopists. Data are lacking on complications of CT colography.

Patient Preferences and Adherence

Some patients report that they find the FOBT unpleasant or difficult to perform, but 50% to 70% of patients will complete FOBT when advised to by a clinician. A reminder system can increase adherence rates by an average of 14%. Studies conducted in primary care settings have found rates of adherence for sigmoidoscopy to be 25% to 50% for the initial test, but there are no data on adherence to repeat examinations. When given information about screening options and offered the choice of FOBT alone, sigmoidoscopy alone, or both tests together, most patients in an academic internal medicine clinic preferred both tests or FOBT alone; only 8% to 13% preferred sigmoidoscopy alone.[27] However, patient adherence to combined testing is lower than it is for sigmoidoscopy or FOBT alone. Patients' acceptance of barium enema screening has not been evaluated.

Studies examining the relative discomfort of barium enema and colonoscopy have produced inconsistent results. In 1 study of patients in a population with considerable previous screening experience, 38% preferred colonoscopy to other methods. The acceptability and feasibility of CT colography have not been examined.

Cost and Cost-effectiveness

Among 6 high-quality cost-effectiveness analyses examining only direct costs, the average cost-effectiveness ratio values for screening adults older than 50 with each of the major strategies were under $30,000 per life-year saved (Year 2000 dollars).[3] Studies varied as to which strategy was most cost-effective, however.

Recommendations of Others

The American Cancer Society recommends screening people at average risk for colorectal cancer beginning at 50 years of age by (1) FOBT annually, (2) flexible sigmoidoscopy every 5 years, (3) annual FOBT plus flexible sigmoidoscopy every 5 years, (4) double-contrast barium enema every 5 years, or (5) colonoscopy every 10 years.[28] The American Cancer Society does not recommend DRE as a stand-alone screening test for colorectal cancer. Similar recommendations are issued by the American College of Surgeons, the American College of Obstetricians and Gynecologists, and the American

Academy of Family Physicians.[29-31] The American Gastroenterological Association, as part of a consortium of related professional organizations, also issues similar recommendations, which are currently being updated.[4] The American College of Physicians–American Society of Internal Medicine does not have current guidelines on screening.[6] The Canadian Task Force on Preventive Health Care concludes that there is good evidence to recommend annual or biennial FOBT and fair evidence to recommend sigmoidoscopy as part of the periodic health examination in average-risk adults after age 50 years; evidence is insufficient to recommend for or against colonosopy or combined FOBT and sigmoidscopy.[32]

References

1. U.S. Preventative Services Task Force. *Guide to Clinical Preventive Services.* 2nd ed. Washington, DC: Office of Disease Prevention and Health Promotion; 1996.
2. Pignone M, Rich M, Teutsch SM, Berg AO, Lohr KN. Screening for colorectal cancer in adults at average risk: a summary of the evidence for the U.S. Preventive Services Task Force. *Ann Intern Med.* 2002;137:132-141.
3. Pignone M, Rich M, Teutsch SM, Berg AO, Lohr KN. *Screening for Colorectal Cancer in Adults.* Systematic Evidence Review No. 7 (Prepared by the Research Triangle Institute-University of North Carolina Evidence-based Practice Center under Contract No. 290-97-0011). Rockville, MD: Agency for Healthcare Research and Quality. June, 2002 (Available on AHRQ Web site at: www.ahrq.gov/clinic/serfiles.htm).
4. Winawer SJ, Fletcher RH, Miller L, et al. Colorectal cancer screening: clinical guidelines and rationale. *Gastroenterology.* 1997;112:594-642.
5. Ries LA, Wingo PA, Miller DS, et al. The annual report to the nation on the status of cancer, 1973-1997, with special section on colorectal cancer. *Cancer.* 2000;88:2398-2424.
6. Stryker SJ, Wolff BG, Culp CE, Libbe SD, Ilstrup DM, MacCarty RL. Natural history of untreated colonic polyps. *Gastroenterology.* 1987;93:1009-1013.
7. Winawer SJ, Shike M. Prevention and control of colorectal cancer. In: Greenwald P, Kramer BS, Weed DL, eds. *Cancer Prevention and Control.* New York: Marcel-Dekker, 1995; 537-560.
8. Yamamoto M, Nakama H. Cost-effectiveness analysis of immunochemical occult blood screening for colorectal cancer among three fecal sampling methods. *Hepatogastroenterology.* 2000;47(32):396-399.
9. Ransohoff DF, Lang CA. Screening for colorectal cancer with the fecal occult blood test: a background paper. American College of Physicians. *Ann Intern Med.* 1997;126(10):811-822.
10. Mandel J, Bond J, Church T, et al. Reducing mortality from colorectal cancer by screening for fecal occult blood. *N Engl J Med.* 1993;328:1365-1371.
11. Hardcastle J, Chamberlain J, Robinson M, et al. Randomised controlled trial of fecal-occult-blood test. *Lancet.* 1996;348:1472-1477.
12. Kronborg O, Fenger C, Olsen J, Jorgensen D, Sondergaard O. Randomised study of screening for colorectal cancer with fecal-occult-blood test. *Lancet.* 1996;348:1467-1471.
13. Atkin WE, Hart A, Edwards R, et al. Uptake, yield of neoplasia, and adverse effects of flexible sigmoidoscopy screening. *Gut.* 1998;42:560-565.
14. Lehman GA, Buchner DM, Lappas JC. Anatomical extent of fiberoptic sigmoidoscopy. *Gastroenterology.* 1983;84:803-808.
15. Winawer SJ, Stewart ET, Zauber AG, et al. A comparison of colonoscopy and double-contrast barium enema for surveillance after polypectomy. *N Engl J Med.* 2000;342:393-397.
16. Rex DK, Cutler CS, Lemmel GT, et al. Colonoscopic miss rates of adenomas determined by back-to-back colonoscopies. *Gastroenterology.* 1997;112:24-28.
17. Mandel JS, Church TR, Ederer F, Bond JH. Colorectal cancer mortality: effectiveness of biennial screening for fecal occult blood. *J Natl Cancer Inst.* 1999;91:434-437.
18. Selby J, Friedman G, Quesenberry C, Weiss N. A case-control study of screening sigmoidoscopy and mortality from colorectal cancer. *N Engl J Med.* 1992;326:653-657.
19. Newcomb PA, Norfleet RG, Storer BE, Surawicz TS, Marcus PM. Screening sigmoidoscopy and colorectal cancer mortality. *J Natl Cancer Inst.* 1992;84:1572-1575.

20. Winawer S. Screening for colorectal cancer with fecal occult blood testing and sigmoidoscopy. *J Natl Cancer Inst.* 1993;85:1311-1318.

21. 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;329:1977-1981.

22. Muller AD, Sonnenberg A. Protection by endoscopy against death from colorectal cancer. A case-control study among veterans. *Arch Intern Med.* 1995;155:1741-1748.

23. Nelson RL, Abcarian H, Prasad ML. Iatrogenic perforation of the colon and rectum. *Dis Colon Rectum.* 1982;25:305-308.

24. Blakeborough A, Sheridan MB, Chapman AH. Complications of barium enema examinations: a survey of UK Consultant Radiologists 1992 to 1994. *Clin Radiol.* 1997;52:142-148.

25. Lieberman DA, Weiss DG, Bond JH, Ahnen DJ, Garewal H, Chejfec G. Use of colonoscopy to screen asymptomatic adults for colorectal cancer. Veterans Affairs Cooperative Study Group 380. *N Engl J Med.* 2000;343:162-168.

26. Imperiale TF, Wagner DR, Lin CY, Larkin GN, Rogge JD, Ransohoff DF. Risk of advanced proximal neoplasms in asymptomatic adults according to the distal colorectal findings. *N Engl J Med.* 2000;343:169-174.

27. Woolf SH. The best screening test for colorectal cancer—a personal choice. *N Engl J Med.* 2000;343:1641-1643.

28. Byers T, Levin B, Rothenberger D, Dodd GD, Smith RA. American Cancer Society guidelines for screening and surveillance for early detection of colorectal polyps and cancer: update 1997. American Cancer Society Detection and Treatment Advisory Group on Colorectal Cancer. *CA Cancer J Clin.* 1997;47(3):154-160. Available at: www.cancer.org/cancerinfo/documents/cancer_10/guidelines.html.

29. Goldstein MM, Messing EM. Prostate and bladder cancer screening. *J Am Coll Surg.* 1987;186(1):63-74. Available at: www.facs.org/dept/jacs/articles/messing.html.

30. American College of Obstetricians and Gynecologists. Primary and preventive care: periodic assessments. ACOG Committee Opinion 246. Washington, DC: ACOG, 2000.

31. American Academy of Family Physicians. Summary of policy recommendations for periodic health examination. Revision 5.0, August 2001, Order No. 962, Reprint No. 510. Available at: www.aafp.org/exam/.

32. Solomon MJ, McLeod RS. Preventive health care, 2001 update. Colorectal cancer screening: recommendations statement. Canadian Task Force on the Periodic Health Examination. *CMAJ.* 2001;15(10):647-660.

Appendix A
U.S. Preventive Services Task Force - Recommendations and Ratings

The Task Force grades its recommendations according to one of 5 classifications (A, B, C, D, I) reflecting the strength of evidence and magnitude of net benefit (benefits minus harms):

A. The USPSTF strongly recommends that clinicians routinely provide [the service] to eligible patients. *The USPSTF found good evidence that [the service] improves important health outcomes and concludes that benefits substantially outweigh harms.*

B. The USPSTF recommends that clinicians routinely provide [the service] to eligible patients. *The USPSTF found at least fair evidence that [the service] improves important health outcomes and concludes that benefits outweigh harms.*

C. The USPSTF makes no recommendation for or against routine provision of [the service]. *The USPSTF found at least fair evidence that [the service] can improve health outcomes but concludes that the balance of benefits and harms is too close to justify a general recommendation.*

D. The USPSTF recommends against routinely providing [the service] to asymptomatic patients. *The USPSTF found at least fair evidence that [the service] is ineffective or that harms outweigh benefits.*

I. The USPSTF concludes that the evidence is insufficient to recommend for or against routinely providing [the service]. *Evidence that [the service] is effective is lacking, of poor quality, or conflicting and the balance of benefits and harms cannot be determined.*

Appendix B
U.S. Preventive Services Task Force - Strength of Overall Evidence

The USPSTF grades the quality of the overall evidence for a service on a 3-point scale (good, fair, poor):

Good: Evidence includes consistent results from well-designed, well-conducted studies in representative populations that directly assess effects on health outcomes.

Fair: Evidence is sufficient to determine effects on health outcomes, but the strength of the evidence is limited by the number, quality, or consistency of the individual studies, generalizability to routine practice, or indirect nature of the evidence on health outcomes.

Poor: Evidence is insufficient to assess the effects on health outcomes because of limited number or power of studies, important flaws in their design or conduct, gaps in the chain of evidence, or lack of information on important health outcomes.

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Summary of Evidence

Note: Separate PDQ summaries on Prevention of Colorectal Cancer [1]; Colon Cancer Treatment [2]; and Rectal Cancer Treatment [3] are also available.

Based on solid evidence, screening for colorectal cancer (CRC) reduces CRC mortality, but there is little evidence that it reduces all cause mortality, possibly because of an observed increase in other causes of death.

Table 1. Effect of Screening Intervention on Reducing Mortality from Colorectal Cancer* Enlarge [4]	**Fecal Occult Blood Test**	**Sigmoidoscopy**	**Digital Rectal Exam**
**There are no data on the effect of other screening interventions (i.e., FOBT/sigmoidoscopy, barium enema, colonoscopy, computed tomographic [CT] colonography, and stool DNA mutation tests) on mortality from colorectal cancer.*			
Study Design	Randomized controlled trials	Case-control studies, randomized controlled trials in progress	Case-control studies
Internal Validity	Good	Fair	Fair
Consistency	Good	Fair	Good
Magnitude of Effects	15%–33%	About 50% for left colon	No effect
External Validity	Fair	Poor	Poor

Table 2. Effect of Screening Intervention on Surrogate Endpoints (e.g., stage at diagnosis, adenoma detection) Enlarge [5]	**Sigmoidoscopy [1,2]**	**FOBT/ Sigmoidoscopy [3,4]**	**Barium Enema [5]**	**Colonoscopy [6,7]**	**CT Colonography [8-10]**	**Stool DNA Mutation Tests [11]**
CT = computed tomography; FOBT = fecal occult blood test.						
Study Design	Case-control studies	Randomized controlled studies	Ecologic and descriptive studies	Ecologic and descriptive studies	Ecologic and descriptive studies	Studies in progress
Internal Validity	Poor	Fair	Fair	Fair	Fair	Unknown
Consistency	Fair	Poor	Poor	Poor	Poor	Unknown
Magnitude	About 45%	No difference	Barium	About 3% of	CT	Unknown

of Effects on Surrogate Endpoints	decrease in detection rate of cancers compared to colonoscopy	in diagnostic yield between sigmoidoscopy + FOBT vs. sigmoidoscopy alone	enema detects about 30%–50% of cancers detected by colonoscopy	patients with no distal adenomas have advanced proximal neoplasia. There is a threefold increase in this rate in patients with distal adenomas.	colonography may have similar sensitivity to colonoscopy in certain centers.	
External Validity	Poor	N/A	N/A	N/A	Poor	Unknown

References

1. Cotterchio M, Manno M, Klar N, et al.: Colorectal screening is associated with reduced colorectal cancer risk: a case-control study within the population-based Ontario Familial Colorectal Cancer Registry. Cancer Causes Control 16 (7): 865-75, 2005. [PUBMED Abstract]

2. Schoenfeld P, Cash B, Flood A, et al.: Colonoscopic screening of average-risk women for colorectal neoplasia. N Engl J Med 352 (20): 2061-8, 2005. [PUBMED Abstract]

3. Segnan N, Senore C, Andreoni B, et al.: Randomized trial of different screening strategies for colorectal cancer: patient response and detection rates. J Natl Cancer Inst 97 (5): 347-57, 2005. [PUBMED Abstract]

4. Gondal G, Grotmol T, Hofstad B, et al.: The Norwegian Colorectal Cancer Prevention (NORCCAP) screening study: baseline findings and implementations for clinical work-up in age groups 50-64 years. Scand J Gastroenterol 38 (6): 635-42, 2003. [PUBMED Abstract]

5. Winawer SJ, Stewart ET, Zauber AG, et al.: A comparison of colonoscopy and double-contrast barium enema for surveillance after polypectomy. National Polyp Study Work Group. N Engl J Med 342 (24): 1766-72, 2000. [PUBMED Abstract]

6. Lieberman DA, Weiss DG, Bond JH, et al.: Use of colonoscopy to screen asymptomatic adults for colorectal cancer. Veterans Affairs Cooperative Study Group 380. N Engl J Med 343 (3): 162-8, 2000. [PUBMED Abstract]

7. Imperiale TF, Wagner DR, Lin CY, et al.: Risk of advanced proximal neoplasms in asymptomatic adults according to the distal colorectal findings. N Engl J Med 343 (3): 169-74, 2000. [PUBMED Abstract]

8. Pickhardt PJ, Choi JR, Hwang I, et al.: Computed tomographic virtual colonoscopy to screen for colorectal neoplasia in asymptomatic adults. N Engl J Med 349 (23): 2191-200, 2003. [PUBMED Abstract]

9. Cotton PB, Durkalski VL, Pineau BC, et al.: Computed tomographic colonography (virtual colonoscopy): a multicenter comparison with standard colonoscopy for detection of colorectal neoplasia. JAMA 291 (14): 1713-9, 2004. [PUBMED Abstract]

10. Mulhall BP, Veerappan GR, Jackson JL: Meta-analysis: computed tomographic colonography. Ann Intern Med 142 (8): 635-50, 2005. [PUBMED Abstract]

11. Imperiale TF, Ransohoff DF, Itzkowitz SH, et al.: Fecal DNA versus fecal occult blood for colorectal-cancer screening in an average-risk population. N Engl J Med 351 (26): 2704-14, 2004. [PUBMED Abstract]

Significance

Colorectal cancer (CRC) is the third most common malignant neoplasm worldwide [1] and the second leading cause of cancer deaths in the United States.[2] It is estimated that there will be 153,760 new cases diagnosed in the United States in 2007 and 52,180 deaths due to this disease.[2] Between 1973 and 1995, mortality from CRC declined by 20.5%, and incidence declined by 7.4% in the United States. The incidence is higher in men than in women. It ranges from 48.3 per 100,000 per year in Hispanic men to 72.5 in African American men. In women it ranges from 32.3 in Hispanics to 56.0 in African Americans per 100,000 per year. The age-adjusted mortality rates for men and women are 24.8 in men and 17.4 in women.[3,4] About 6% of Americans are expected to develop the disease within their lifetime.[3] Age-specific incidence and mortality rates show that most cases are diagnosed after 50 years of age.[3]

Among the groups that have a high incidence of CRC are those with hereditary conditions, such as familial adenomatous polyposis and hereditary nonpolyposis CRC (inherited in an autosomal dominant manner). Combined, the two groups account for no more than 6% of CRCs. More common conditions associated with an increased risk include a personal history of CRC or adenomas; first-degree relative with CRC; first-degree relative with adenomas diagnosed before 60 years of age;[5] a personal history of ovarian, endometrial, or breast cancer; and a personal history of long-standing chronic ulcerative colitis or Crohn colitis.[6-8] These high-risk groups account for about a quarter of all CRCs. Limiting screening or early cancer detection to only these high-risk groups would miss the majority of CRCs.[9]

Genetic,[10] experimental, and epidemiologic [11] studies suggest that CRC results from complex interactions between inherited susceptibility and environmental or lifestyle factors. Efforts to identify causes and to develop effective preventive measures led to the hypothesis that adenomatous polyps (adenomas) are precursors for the vast majority of CRCs.[12] In effect, measures that reduce the incidence and prevalence of adenomas may result in a subsequent decrease in the risk of CRC.[13] In addition, the formation and spontaneous regression of adenomas may also be a dynamic process.[14]

References

1. Shike M, Winawer SJ, Greenwald PH, et al.: Primary prevention of colorectal cancer. The WHO Collaborating Centre for the Prevention of Colorectal Cancer. Bull World Health Organ 68 (3): 377-

85, 1990. [PUBMED Abstract]

2. American Cancer Society.: Cancer Facts and Figures 2007. Atlanta, Ga: American Cancer Society, 2007. Also available online [6]. Last accessed December 20, 2007.

3. Ries LAG, Eisner MP, Kosary CL, et al., eds.: SEER Cancer Statistics Review, 1975-2002. Bethesda, Md: National Cancer Institute, 2005. Also available online [7]. Last accessed December 19, 2007.

4. Edwards BK, Howe HL, Ries LA, et al.: Annual report to the nation on the status of cancer, 1973-1999, featuring implications of age and aging on U.S. cancer burden. Cancer 94 (10): 2766-92, 2002. [PUBMED Abstract]

5. Ahsan H, Neugut AI, Garbowski GC, et al.: Family history of colorectal adenomatous polyps and increased risk for colorectal cancer. Ann Intern Med 128 (11): 900-5, 1998. [PUBMED Abstract]

6. Fuchs CS, Giovannucci EL, Colditz GA, et al.: A prospective study of family history and the risk of colorectal cancer. N Engl J Med 331 (25): 1669-74, 1994. [PUBMED Abstract]

7. Smith RA, von Eschenbach AC, Wender R, et al.: American Cancer Society guidelines for the early detection of cancer: update of early detection guidelines for prostate, colorectal, and endometrial cancers. Also: update 2001--testing for early lung cancer detection. CA Cancer J Clin 51 (1): 38-75; quiz 77-80, 2001 Jan-Feb. [PUBMED Abstract]

8. Levin B, Rozen P, Young GP: How should we follow up colorectal premalignant conditions? In: Rozen P, Young G, Levin B, et al.: Colorectal Cancer in Clinical Practice: Prevention, Early Detection, and Management. London, UK: Martin Dunitz, 2002, pp 67-76.

9. Winawer SJ, Fletcher RH, Miller L, et al.: Colorectal cancer screening: clinical guidelines and rationale. Gastroenterology 112 (2): 594-642, 1997. [PUBMED Abstract]

10. Fearon ER, Vogelstein B: A genetic model for colorectal tumorigenesis. Cell 61 (5): 759-67, 1990. [PUBMED Abstract]

11. Young GP, Rozen P, Levin B: How does colorectal cancer develop? In: Rozen P, Young G, Levin B, et al.: Colorectal Cancer in Clinical Practice: Prevention, Early Detection, and Management. London, UK: Martin Dunitz, 2002, pp 23-37.

12. Muto T, Bussey HJ, Morson BC: The evolution of cancer of the colon and rectum. Cancer 36 (6): 2251-70, 1975. [PUBMED Abstract]

13. Winawer SJ, Zauber AG, Ho MN, et al.: Prevention of colorectal cancer by colonoscopic polypectomy. The National Polyp Study Workgroup. N Engl J Med 329 (27): 1977-81, 1993. [PUBMED Abstract]

14. Loeve F, Boer R, Zauber AG, et al.: National Polyp Study data: evidence for regression of adenomas. Int J Cancer 111 (4): 633-9, 2004. [PUBMED Abstract]

Evidence of Benefit

Fecal Occult Blood Test

There are five controlled clinical trials that have been completed or that are in progress to evaluate the efficacy of screening utilizing the fecal occult blood test (FOBT). The Swedish trial is a targeted study for the group aged 60 to 64 years.[1] The English program selects candidates from lists of family practitioners.[2] The Danish trial offers screening to a population aged 45 to 75 years randomly assigned to a control and a study group.[3,4] The Memorial Sloan-Kettering Cancer Center-Strang Clinic (MSKCC) trial, completed in 1985, was an evaluation of the FOBT as a supplement to annual rigid sigmoidoscopy.[5] The study and control groups were selected by calendar periods.

The Minnesota trial demonstrated that annual FOBT testing using primarily rehydrated samples decreased mortality from CRC by 33% [6] and that biennial testing developed a 21% relative mortality reduction.[7] A large part of the reduction may be attributed to chance detection of cancer by colonoscopies; rehydration of guaiac test slides greatly increased positivity and consequently increased the number of colonoscopies performed.[8] Subsequent analyses by the Minnesota investigators using mathematical modeling suggested that for 75% to 84% of the patients mortality reduction was achieved because of sensitive detection of CRCs by the test; chance detection played a minor role (16%–25% of the reduction).[9] Nearly 85% of patients with a positive test underwent diagnostic procedures that included colonoscopy or double-contrast barium enema plus flexible sigmoidoscopy (FS). After 18 years of follow-up, the incidence of CRC was reduced by 20% in the annually screened arm and 17% in the biennially screened arm.[10]

The English trial allocated approximately 76,000 individuals to each arm. Those in the screened arm were offered nonrehydrated FOBT testing every 2 years for three to six rounds from 1985 to 1995. Median follow-up time was 7.8 years. Sixty percent completed at least one test; 38% completed all tests. Cumulative incidence of CRC was similar in both arms. The trial reported a relative risk reduction of 15% in CRC mortality (odds ratio [OR] = 0.85; 95% confidence interval [CI], 0.74–0.98).[11] In this study, the serious complication rate of colonoscopy was 0.5 %. There were five deaths within 30 days of surgery for screen-detected CRC or adenoma out of a total of 75,253 individuals screened.[12] After a median follow-up of 11.8 years, a difference in CRC incidence between the intervention and control groups was not observed. Overall, the disease-specific mortality-rate-ratio associated with screening was 0.87 (0.78–0.97, P = .01). The rate ratio for death from all causes was 1.00 (0.98–1.02, P = .79).[13]

The Danish trial in Funen, Denmark, entered approximately 31,000 individuals into each of two arms, in which individuals in the screened arm were offered nonrehydrated FOBT testing every 2 years for nine rounds over a 17-year period. Sixty-seven percent completed the first screen, and more than 90% of individuals invited to each subsequent screen underwent FOBT testing. This trial demonstrated an 18% reduction in CRC mortality at 10 years of follow-up,[14] 15% at 13 years of follow-up (relative risk [RR] = 0.85; 95% CI, 0.73–1.00),[15] and 11% at 17 years of follow-up (RR = 0.89; 95% CI, 0.78–1.01).[16] CRC incidence and overall mortality was virtually identical in both arms.

All trials have shown a more favorable stage distribution in the screened population compared with controls (Table 3 [8]). For example, data from the Danish trial indicate that while the cumulative incidence of CRC was similar in the screened and control groups, a higher percentage of CRCs and adenomas were Dukes A and B lesions in the screened group.[14] A meta-analysis of all previously reported randomized trials using biennial

FOBT showed no overall mortality reduction by FOBT screening (RR = 1.002; 95% CI, 0.989–1.085). The RR of CRC death in the FOBT arm was 0.87 (95% CI, 0.8–0.95), and the RR of non-CRC death in the FOBT group was 1.02 (95% CI, 1.00–1.04, *P* = .015).[17]

The MSKCC study evaluated compliance and effectiveness, in a setting of comprehensive medical examinations, of using the FOBT in conjunction with sigmoidoscopy to screen for CRC. From 1975 to 1979, a total of 21,756 patients (aged 40 years and older) who presented at the Preventive Medicine Institute-Strang Clinic for routine medical evaluations were enrolled by calendar period into study and control groups. Study patients were offered annually both rigid sigmoidoscopy examinations and FOBTs requiring two stool specimens per day for 3 days, while control patients were offered only annual sigmoidoscopy. Trial I was primarily a demonstration of feasibility of using the FOBT as a supplemental screening method. Trial II was an evaluation of effectiveness. In Trial II, CRC mortality was lower in the study group than in the control group (0.36 vs. 0.63 per 1,000), a nonstatistically significant result (*P* = .053).

Mathematical models have been constructed to extrapolate the results of screening trials to screening programs for the general population in community health care delivery settings. These models project a reduction in CRC mortality or an increase in life expectancy using currently available screening methodology.[18-21] The anticipated success of such methodology is critically dependent on the appropriate use of the FOBT and an effective clinical management plan.[22,23]

A systematic review done through the Cochrane Collaboration examined all CRC screening randomized trials that involved FOBT testing on more than one occasion. The combined results showed that trial participants allocated to screening had a 16% lower CRC mortality (RR = 0.84; 95% CI, 0.78–0.90). There was, however, no difference in all-cause mortality between the screened and control groups (RR = 1.00; 95% CI, 0.99–1.02). Furthermore, the trials reported a low positive predictive value for the FOBT test, suggesting that more than 80% of all positive tests were false-positives.[24]

In general, on initial (prevalence) examinations, from 1% to 5% of unselected persons tested with FOBT have positive test results. Of those with positive test results, approximately 2% to 10% have cancer and approximately 20% to 30% have adenomas,[25,26] depending on how the test is done. Data from randomized controlled trials are summarized in Table 3.

Table 3. Randomized Controlled Screening Trials: Fecal Occult Blood Testing Enlarge [9] **Site**	**Population Size**	**Positivity Rate (%)**	*** % Localized**		**Testing Interval**	**Relative Mortality Reduction**
** % Localized = T1–3 N0 M0.*						
			Screened	**Control**		
Minnesota [6,7]	48,000	unrehydrated: 2.4%	59	53	Annual	33%
		rehydrated:			Biennial	21%

		9.8%				
United Kingdom [11]	150,000	unrehydrated: 2.1%	52	44	Biennial	15%
Denmark [14]	62,000	unrehydrated: 1.0%	56	48	Biennial	18%
Sweden [1]	27,000	unrehydrated: 1.9%	65	33		not available
		rehydrated: 5.8%				

Newer FOBTs: Nonrandomized Controlled Trial Evidence

Newer FOBTs have been developed to detect human hemoglobin (immunochemical fecal occult blood test or iFOBT) in contrast to the peroxidase-like activity that is detected by the guaiac-based FOBT (gFOBT) studied in the randomized controlled trials above.

In a study of 1,000 persons having a colonoscopy and iFOBT done on three bowel movements, the sensitivity and specificity for CRC was 94% and 87%; for advanced adenoma and CRC, it was 67% and 91%.[27] In another study using a different iFOBT, tested in one bowel movement, the sensitivity for CRC was 66% and for advanced adenoma and CRC, the sensitivity was 27%; specificity was 95%.[28] These sensitivities are much higher than the 13% to 39% sensitivity for CRC using gFOBT when studied in a similar way.

Sigmoidoscopy

The flexible fiberoptic sigmoidoscope was introduced in 1969. The 60 cm flexible sigmoidoscope became available in 1976.[29] The flexible sigmoidoscope permits a more complete examination of the distal colon with more acceptable patient tolerance than the older rigid sigmoidoscope. The rigid instrument can discover 25% of polyps, and the 60 cm scope can find as many as 65%. The finding of an adenoma by FS may warrant colonoscopy to evaluate the more proximal portion of the colon.[30,31] The prevalence of advanced proximal neoplasia is increased in patients with a villous or tubulovillous adenoma distally and is also increased in those 65 years or older with a positive family history of CRC and with multiple distal adenomas.[32] Removal of adenomas is associated with a decreased risk of subsequent CRC.[33] While most of these adenomas are polypoid, flat and depressed lesions may be more prevalent than previously recognized. Large flat and depressed lesions are more likely to be severely dysplastic. Specialized techniques may be needed to identify, biopsy, and remove such lesions.[34]

Virtually all screening studies using these types of sigmoidoscopes have demonstrated an increase in the proportion of early cases and a corresponding increase in survival compared with cases diagnosed in a nonscreening environment. Most of these studies, however, lack appropriate comparison groups, and their interpretation is unclear because of screening biases.

The Memorial-Strang Clinic sigmoidoscopy study was conducted between 1946 and 1954 in 26,124 patients.[35] The survival rate in the 58 patients found to have cancer was 90% after a follow-up period of 15

years. There were, however, neither controls nor adjustment for biases.

One study was conducted over a 25-year period with 18,158 patients who underwent periodic rigid sigmoidoscopy with removal of polyps.[36] This study showed a significant reduction in the incidence of cancer in the rectosigmoid colon when compared with statewide data. There were 14 rectal cancers in the study group, which was only 15% of the expected incidence in that state. This study, however, was not controlled and provided minimal follow-up data.

The Kaiser-Permanente Multiphasic Health Checkup was a randomized study of 10,713 health plan members between the ages of 35 and 54 years; after 16 years, the study reported a more favorable stage distribution and survival rate and a reduction in mortality between the study and control groups (12 vs. 29 deaths), which was statistically significant.[37] In a re-evaluation considering only those cancers within reach of the sigmoidoscope, no statistical difference, however, could be demonstrated.

Two case-control studies have been reported that evaluate the efficacy of screening sigmoidoscopy in preventing CRC mortality;[38,39] one study used rigid sigmoidoscopy, and the other used rigid and FS. Both studies were conducted in prepaid health plans and suggested a significantly decreased risk (70%–90%) of fatal cancer of the distal colon or rectum among individuals with a history of one or more sigmoidoscopic examinations compared with nonscreened patients. In a multicenter study of colon cancer in northern California and Utah, sigmoidoscopic screening was associated with a decreased incidence of colon cancer in both men (OR = 0.56; 95% CI, 0.44–0.77) and women (OR = 0.53; 95% CI, 0.33–0.77) after adjusting for other risk factors for colon cancer.[40] A population-based mass screening program with proctoscopy for CRC in one Chinese province was associated with a reduction in incidence and mortality from rectal cancer. Mortality decreased from 4.20 (in 1974–1976) per 100,000 to 2.98 (in 1992–1996) per 100,000.[41]

In a population-based, case-control study in Germany, 39%, 77%, and 64% of proximal, distal, and total CRCs, respectively, were estimated to be preventable by colonoscopy. The estimated proportion of total CRCs preventable by sigmoidoscopy was 45% among both women and men, assuming that sigmoidoscopy reaches the junction of the descending and sigmoid colon only and that findings of distal polyps are not followed by colonoscopy. Assuming that sigmoidoscopy reaches the splenic flexure and colonoscopy is done after detection of distal polyps, estimated proportions of total CRCs preventable by sigmoidoscopy increased to 50% and 55% (73% and 91% of total CRCs preventable by primary colonoscopy) among women and men, respectively.

Based on an extensive evidence-based review, guidelines have been formulated by representatives from a consortium of medical societies for screening and surveillance of those at average risk and those at increased risk for CRC because of a family history of CRC or genetic syndromes or a personal history of adenomatous polyps, inflammatory bowel disease, or curative-intent resection of CRC.[42] Adherence to screening by FOBT and sigmoidoscopy is below 50% in unselected population studies.[43] Among research volunteers in a large-scale randomized clinical trial of screening, more than 85% accepted repeat sigmoidoscopy after 3 years. An uncomfortable or technically inadequate initial examination, which may be more common in women, had an adverse effect on subsequent adherence.[44,45]

An optimal frequency for CRC screening has not been rigorously established. Various organizations have recommended a 5-year interval for repeat sigmoidoscopy based on data from observational studies.[46,47] One case-control study found a negative association between sigmoidoscopy and mortality that persisted for

as many as 10 years,[38] while another case-control study of endoscopy found an effect only for as many as 6 years. In contrast, other studies have examined the yield of adenomas [48] and cancers [48,49] in the distal colon 3 years after a negative sigmoidoscopy.[48] After only 3 years, potentially dangerous neoplasms were discovered; 72 advanced adenomas and 6 cancers were identified among 9,317 individuals examined.

Combination of FOBT and Flexible Sigmoidoscopy

In 2,885 veterans (97% male; mean age 63 years), the prevalence of advanced adenoma at colonoscopy was 10.6%. It was estimated that combined screening with one-time fecal occult blood test and sigmoidoscopy would detect 75.8% (95% CI, 71.0%–80.6%) of advanced neoplasms. Examination of the rectum and sigmoid colon during colonoscopy was defined as a surrogate for sigmoidoscopy. This represented a small but statistically insignificant increase in rate of detection of advanced neoplasia when compared with FS alone (70.3%; 95% CI, 65.2%–75.4%). The latter result could be achieved assuming that all patients with an adenoma in the distal colon undergo complete colonoscopy. Advanced neoplasia was defined as a lesion measuring at least 10 mm in diameter, containing 25% or more villous histology, high-grade dysplasia, or invasive cancer.[50] One-time use of FOBT differs from the annual or biennial application reported in those studies summarized in Table 1.

The Norwegian Colorectal Cancer Prevention once-only screening study randomly assigned 20,780 men and women, aged 50 to 64 years, to FS only or a combination of FS and FOBT with FlexSure OBT.[51] A positive FS was defined as a finding of any neoplasia or any polyp at least 10.0 mm. A positive FS or FOBT qualified for colonoscopy. Attendance in this study was 65%. Forty-one cases of CRC were detected (0.3% of screened individuals). Any adenoma was found in 2,208 participants (17%), and 545 (4.2%) had high-risk adenomas. There was no difference in diagnosis yield between the FS and the FS and FOBT groups regarding CRC or high-risk adenoma. There were no serious complications after FS, but there were six perforations after therapeutic colonoscopy (1:336).

Barium Enema

As part of the National Polyp Study, colonoscopic examination and barium enema were compared in paired surveillance examinations in those who had undergone a prior colonoscopic polypectomy.[52] The proportion of examinations in which adenomatous polyps were detected by barium enema was related to the size of the adenoma ($P = .009$); the rate was 32% for colonoscopic examinations in which the largest adenomas detected were no larger than 5.0 mm, 53% for those in which the largest adenomas detected were 6.0 mm to 10.0 mm, and 48% for those in which the largest adenomas detected were larger than 10.0 mm. In patients who have undergone colonoscopic polypectomy, colonoscopic examination is a more sensitive method of surveillance than double-contrast barium enema.

Colonoscopy

In a colonoscopic study of 3,121 predominantly male U.S. veterans (mean age: 63 years), advanced neoplasia (defined as an adenoma that was ≥10.0 mm in diameter, a villous adenoma, an adenoma with high-grade dysplasia, or invasive cancer) was identified in 10.5% of the individuals.[53] Among patients with no adenomas distal to the splenic flexure, 2.7% had advanced proximal neoplasia. Patients with large adenomas

1.7–4.1). One half of those with advanced proximal neoplasia, however, had no distal adenomas. In a study of 1,994 adults (aged 50 years or older) who underwent colonoscopic screening as part of a program sponsored by an employer, 5.6% had advanced neoplasms.[54] Forty-six percent of those with advanced proximal neoplasms had no distal polyps (hyperplastic or adenomatous). If colonoscopic screening is performed only in patients with distal polyps, about half the cases of advanced proximal neoplasia will not be detected.

A study of colonoscopy in women compared the yield of sigmoidoscopy versus colonoscopy. Among 1,463 women, cancer was found in one and advanced colonic neoplasia in 72 women or 4.9% (about one half the prevalence compared with men). The authors focused, however, on RR (i.e., RR of missing an advanced neoplasm) as the outcome, instead of absolute risk of such neoplasms, which is substantially lower in women. In addition, the natural history of advanced neoplasia is not known, so its importance as an outcome in studies of detection is not clear.[55]

Analysis of data from a colonoscopy-based screening program in Warsaw, Poland demonstrated higher rates of advanced neoplasia in men than in women. The predominant age range of participants was 50 to 66 years. Of the 43,042 participants aged 50 to 66 years, advanced neoplasia was detected in 5.9% (5.7% among women with a family history of CRC; 4.3% among women without a family history of CRC; 12.2% among men with a family history; and 8.0% among men without a family history of CRC). Clinically significant complications requiring medical intervention were rare (0.1%) consisting of 5 perforations, 13 episodes of bleeding, 22 cardiovascular events, and 11 other events over the entire population of 50,148 screened persons. There were no deaths; however, the author reported that collection of 30-day complications data was not systematic (therefore, the data may not be reliable).[56]

Detection rates in colonoscopy screening vary with the rate at which the endoscopist examines the colon while withdrawing the scope. Detection rates among gastroenterologists (mean number of lesions per patient screened, 0.10 to 1.05; range of the percentage of patients with adenomas, 9.4% to 23.7%) and times to withdraw (3.1 to 16.8 minutes for procedures not including polyp removal). Examiners whose mean withdrawal time was 6 minutes or more had higher detection rates than those with mean withdrawal times of less than 6 minutes (28.3% vs. 11.8%; $P < .001$ for any neoplasia) and (6.4% vs. 2.6%; $P < .005$ for advanced neoplasia).[57]

Virtual Colonoscopy (Computed Tomographic Colonography)

Virtual colonoscopy (also known as computed tomographic [CT] colonography or CT pneumocolon) refers to the examination of computer-generated images of the colon constructed from data obtained from an abdominal CT examination. These images simulate the effect of a conventional colonoscopy. Patients must take laxatives to clean the colon before the procedure, and the colon is insufflated with air (sometimes carbon dioxide) by insertion of a rectal tube just prior to radiographic examination.[58]

The performance of virtual colonoscopy depends heavily on the size of the target lesion. In a series of 300 patients who were referred for CRC screening or the evaluation of symptoms and who underwent CT colonography followed by conventional colonoscopy, investigators obtained sensitivities for CT colonography of 90% for 83 polyps measuring larger than 10.0 mm and 80% for 141 polyps measuring 5.0 to 9.9 mm. The per patient sensitivity for the 10.0 mm lesion size was 94% (64 of 68), and it was 66.9% (95 of 142) for adenomas smaller than 5.0 mm. CT colonography led to false identification of 45 polyps ranging in size from 3.0 mm to 17.0 mm in patients who had normal colonoscopic results. Overall performance

characteristics for CT colonography were similar when comparing results for the 96 individuals without symptoms to results for the 204 symptomatic individuals.[59]

In a separate series of 201 patients who had symptoms suggestive of colorectal disease or who were undergoing surveillance because of prior colorectal neoplasia, investigators found that CT colonography detected all 13 CRCs identified in 13 patients on (endoscopic) colonoscopy, but only 20 (7 > 10.0 mm) of the 118 (14 > 10.0 mm) polyps in 63 patients. Sensitivity for detection of invasive carcinoma and/or polyps 10.0 mm or larger in diameter was 73% (95% CI, 56%–90%), and the specificity was 94% (95% CI, 91%–98%).[60]

One thousand two hundred thirty-three asymptomatic adults underwent complete virtual and optical colonoscopic examinations (728 men and 505 women; mean age 57.8 years) at several U.S. institutions employing an identical state-of-the-art protocol between May 2002 and June 2003. Extraordinary care was given to bowel preparation, and stool tagging was employed to minimize artifacts. High-speed, thin-section, supine-position and prone-position, single breath-hold scans were reconstructed in both two dimensions (2-D) and three dimensions (3-D), but the 3-D data were relied upon for image interpretation, using commercially available software.

Polyps were measured with electronic calipers and recorded according to colonic segment. Extracolonic findings were also recorded. CT colonographic studies were prospectively interpreted by one of six board-certified radiologists, each previously trained on a minimum of 25 CT colonographic studies, immediately before optical colonoscopic examination. Optical colonoscopies were performed by 17 experienced gastroenterologists or colorectal surgeons who were initially unaware of the CT findings. Polyps were photographed and measured with a calibrated linear probe.

CT results were unblinded segment by segment to the colonoscopists to allow them to re-evaluate their findings in light of the additional CT information, and thereby create a reference standard against which both CT colonography and optical colonoscopy findings could be compared. Performance characteristics for CT (and optical) colonoscopy were calculated for adenomatous polyps. Sensitivity of CT colonography increased from 88.7% (149/168), for adenomas at least 6.0 mm, to 93.8% (45/48), for adenomas at least 10.0 mm, with respective specificities of 79.6% and 96.0%. (Sensitivities for optical colonoscopy in the absence of CT information were, respectively, by size 92.3% and 87.5%.)

Most of the polyps found on CT colonography, but not on the initial optical colonoscopy, were situated behind a colonic fold, that is “recognized as a relative blind spot” for optical colonoscopy. Interobserver agreement for independent double readings of CT colonography studies, segment by segment, was good, 99.6% for polyps at least 10.0 mm and 97.6% for polyps at least 6.0 mm. Only two cancers were detected in this asymptomatic population, one by optical colonoscopy and both by CT colonography. Fifty-six patients (4.5%) had extracolonic findings considered to be potentially clinically important and needing medical workup.[61]

Another study reported very different results. This study was a prospective evaluation of CT colonography among 600 participants who were seen at nine large medical centers. The participants were referred for routine clinically indicated colonoscopy, and CT colonography was performed immediately prior to the colonoscopy using multidetector scanning. The accuracy of CT colonography was substantially lower than previously reported; 39% of lesions less than 6 mm and 55% of lesions less than 1 cm were detected and six

out of eight cancers were detected using CT colonography. Additionally, the accuracy of CT colonography varied substantially among centers and did not improve over time. Of note, some of the imaging techniques used in previously published reports were not used in this study, and that might explain, in part, the low sensitivity of the test in this report. The authors conclude, however, that techniques and training need to be improved before widespread use because most clinically significant polyps were missed.[62]

A study has assessed how well virtual colonoscopy can detect colorectal polyps without a laxative prep. The question is of great importance for implementation because the laxative prep required by both conventional colonoscopy, and virtual colonoscopy is considered a great disadvantage by patients. By tagging feces with iodinated contrast material ingested during several days prior to the procedure, investigators were able to detect lesions larger than 8 mm with 95% sensitivity and 92% specificity.[63] The particular tagging material used in this study caused about 10% of patients to become nauseated, however, other materials are being assessed. While a number of hurdles remain to be overcome before virtual colonoscopy becomes popular and widely used,[64] this study provides important preliminary data suggesting that the problem of laxative preparation might be successfully addressed.

Extracolonic abnormalities are common in CT colonography. Fifteen percent of patients in an Australian series of 100 patients, referred for colonography because of symptoms or family history, were found to have extracolonic findings, 11 needing further medical workups for renal, splenic, uterine, liver, and gallbladder abnormalities.[65] In another study, 59% of 111 symptomatic patients referred for clinical colonoscopy in a Swedish hospital between June 1998 and September 1999 were found to have moderate or major extracolonic conditions on CT colonography. CT colonography was performed immediately prior to colonoscopy and these findings required further evaluation. It is unstated to what extent the follow-up of these incidental findings benefited patients.[66]

Sixty-nine percent of 681 asymptomatic patients in Minnesota had extracolonic findings, of which 10% were considered to be “highly important” by the investigators, requiring further medical workup. Suspected abnormalities involved kidney (34), chest (22), liver (8), ovary (6), renal or splenic arteries (4), retroperitoneum (3), and pancreas (1);[67] however, the extent to which these findings will contribute to benefits or harms is uncertain.

Technical improvements involving both the interpretation methodology, such as 3-D imaging, and bowel preparation are under study in many centers. While specificity for detection of polyps is homogeneously high in many studies, sensitivity can vary widely. These variations are attributable to a number of factors including characteristics of the CT scanner and detector, width of collimation, mode of imaging (2-D vs. 3-D and/or "fly-through"), as well as variability in expertise of radiologists.[68]

Digital Rectal Examination

A case-control study reported that routine digital rectal examination was not associated with any statistically significant reduction in mortality from distal rectal cancer.[69]

Detection of DNA Mutations in the Stool

these gene mutations that have been shed into the stool.[71-74] Stool DNA testing was recently assessed in a prospective study of asymptomatic persons who received colonoscopy, 3-card FOBT (Hemoccult II), and stool DNA testing based on a panel of markers assessing 21 mutations. Conducted in a blinded way with prestated hypotheses and analyses, the study found that among 4,404 patients, the DNA panel had a sensitivity for CRC of 51.6% (for all stages of CRC) versus 12.9% for Hemoccult II, while the false-positive rates were 5.6% and 4.8%, respectively. On this basis, the approach looks promising but would be improved, if possible, by increased sensitivity (perhaps by increasing the number of DNA markers) and by reduced cost.[75,76]

References

1. Kewenter J, Björk S, Haglind E, et al.: Screening and rescreening for colorectal cancer. A controlled trial of fecal occult blood testing in 27,700 subjects. Cancer 62 (3): 645-51, 1988. [PUBMED Abstract]

2. Hardcastle JD, Thomas WM, Chamberlain J, et al.: Randomised, controlled trial of faecal occult blood screening for colorectal cancer. Results for first 107,349 subjects. Lancet 1 (8648): 1160-4, 1989. [PUBMED Abstract]

3. Kronborg O, Fenger C, Søndergaard O, et al.: Initial mass screening for colorectal cancer with fecal occult blood test. A prospective randomized study at Funen in Denmark. Scand J Gastroenterol 22 (6): 677-86, 1987. [PUBMED Abstract]

4. Kronborg O, Fenger C, Olsen J, et al.: Repeated screening for colorectal cancer with fecal occult blood test. A prospective randomized study at Funen, Denmark. Scand J Gastroenterol 24 (5): 599-606, 1989. [PUBMED Abstract]

5. Winawer SJ, Flehinger BJ, Schottenfeld D, et al.: Screening for colorectal cancer with fecal occult blood testing and sigmoidoscopy. J Natl Cancer Inst 85 (16): 1311-8, 1993. [PUBMED Abstract]

6. Mandel JS, Bond JH, Church TR, et al.: Reducing mortality from colorectal cancer by screening for fecal occult blood. Minnesota Colon Cancer Control Study. N Engl J Med 328 (19): 1365-71, 1993. [PUBMED Abstract]

7. Mandel JS, Church TR, Ederer F, et al.: Colorectal cancer mortality: effectiveness of biennial screening for fecal occult blood. J Natl Cancer Inst 91 (5): 434-7, 1999. [PUBMED Abstract]

8. Lang CA, Ransohoff DF: Fecal occult blood screening for colorectal cancer. Is mortality reduced by chance selection for screening colonoscopy? JAMA 271 (13): 1011-3, 1994. [PUBMED Abstract]

9. Ederer F, Church TR, Mandel JS: Fecal occult blood screening in the Minnesota study: role of chance detection of lesions. J Natl Cancer Inst 89 (19): 1423-8, 1997. [PUBMED Abstract]

10. Mandel JS, Church TR, Bond JH, et al.: The effect of fecal occult-blood screening on the incidence of colorectal cancer. N Engl J Med 343 (22): 1603-7, 2000. [PUBMED Abstract]

11. Hardcastle JD, Chamberlain JO, Robinson MH, et al.: Randomised controlled trial of faecal-occult-blood screening for colorectal cancer. Lancet 348 (9040): 1472-7, 1996. [PUBMED Abstract]

12. Robinson MH, Hardcastle JD, Moss SM, et al.: The risks of screening: data from the Nottingham randomised controlled trial of faecal occult blood screening for colorectal cancer. Gut 45 (4): 588-92, 1999. [PUBMED Abstract]

13. Scholefield JH, Moss S, Sufi F, et al.: Effect of faecal occult blood screening on mortality from colorectal cancer: results from a randomised controlled trial. Gut 50 (6): 840-4, 2002. [PUBMED Abstract]

14. Kronborg O, Fenger C, Olsen J, et al.: Randomised study of screening for colorectal cancer with faecal-occult-blood test. Lancet 348 (9040): 1467-71, 1996. [PUBMED Abstract]

15. Jørgensen OD, Kronborg O, Fenger C: A randomised study of screening for colorectal cancer using faecal occult blood testing: results after 13 years and seven biennial screening rounds. Gut 50 (1): 29-32, 2002. [PUBMED Abstract]

16. Kronborg O, Jørgensen OD, Fenger C, et al.: Randomized study of biennial screening with a faecal occult blood test: results after nine screening rounds. Scand J Gastroenterol 39 (9): 846-51, 2004. [PUBMED Abstract]

17. Moayyedi P, Achkar E: Does fecal occult blood testing really reduce mortality? A reanalysis of systematic review data. Am J Gastroenterol 101 (2): 380-4, 2006. [PUBMED Abstract]

18. Gyrd-Hansen D, Søgaard J, Kronborg O: Colorectal cancer screening: efficiency and effectiveness. Health Econ 7 (1): 9-20, 1998. [PUBMED Abstract]

19. Loeve F, Boer R, van Oortmarssen GJ, et al.: The MISCAN-COLON simulation model for the evaluation of colorectal cancer screening. Comput Biomed Res 32 (1): 13-33, 1999. [PUBMED Abstract]

20. Wagner JL, Tunis S, Brown M, et al.: Cost-effectiveness of colorectal cancer screening in average-risk adults. In: Young GP, Rozen P, Levin B, eds.: Prevention and Early Detection of Colorectal Cancer. London, England: WB Saunders, 1996, pp 321-356.

21. Whynes DK, Neilson AR, Walker AR, et al.: Faecal occult blood screening for colorectal cancer: is it cost-effective? Health Econ 7 (1): 21-9, 1998. [PUBMED Abstract]

22. Suggested technique for fecal occult blood testing and interpretation in colorectal cancer screening. American College of Physicians. Ann Intern Med 126 (10): 808-10, 1997. [PUBMED Abstract]

23. Ransohoff DF, Lang CA: Screening for colorectal cancer with the fecal occult blood test: a background paper. American College of Physicians. Ann Intern Med 126 (10): 811-22, 1997. [PUBMED Abstract]

24. Hewitson P, Glasziou P, Irwig L, et al.: Screening for colorectal cancer using the faecal occult blood test, Hemoccult. Cochrane Database Syst Rev (1): CD001216, 2007. [PUBMED Abstract]

25. Eddy DM: Screening for colorectal cancer. Ann Intern Med 113 (5): 373-84, 1990. [PUBMED Abstract]

26. Allison JE, Feldman R, Tekawa IS: Hemoccult screening in detecting colorectal neoplasm: sensitivity, specificity, and predictive value. Long-term follow-up in a large group practice setting. Ann Intern Med 112 (5): 328-33, 1990. [PUBMED Abstract]

27. Levi Z, Rozen P, Hazazi R, et al.: A quantitative immunochemical fecal occult blood test for colorectal neoplasia. Ann Intern Med 146 (4): 244-55, 2007. [PUBMED Abstract]

28. Morikawa T, Kato J, Yamaji Y, et al.: A comparison of the immunochemical fecal occult blood test and total colonoscopy in the asymptomatic population. Gastroenterology 129 (2): 422-8, 2005. [PUBMED Abstract]

29. Fath RB, Winawer SJ: Endoscopic screening by flexible fiberoptic sigmoidoscopy. Front Gastrointest Res 10: 102-111, 1986.

30. Read TE, Read JD, Butterly LF: Importance of adenomas 5 mm or less in diameter that are detected by sigmoidoscopy. N Engl J Med 336 (1): 8-12, 1997. [PUBMED Abstract]

31. Wallace MB, Kemp JA, Trnka YM, et al.: Is colonoscopy indicated for small adenomas found by screening flexible sigmoidoscopy? Ann Intern Med 129 (4): 273-8, 1998. [PUBMED Abstract]

32. Levin TR, Palitz A, Grossman S, et al.: Predicting advanced proximal colonic neoplasia with screening sigmoidoscopy. JAMA 281 (17): 1611-7, 1999. [PUBMED Abstract]

33. Winawer SJ, Zauber AG, Ho MN, et al.: Prevention of colorectal cancer by colonoscopic polypectomy. The National Polyp Study Workgroup. N Engl J Med 329 (27): 1977-81, 1993. [PUBMED Abstract]

34. Rembacken BJ, Fujii T, Cairns A, et al.: Flat and depressed colonic neoplasms: a prospective study of 1000 colonoscopies in the UK. Lancet 355 (9211): 1211-4, 2000. [PUBMED Abstract]

35. Hertz RE, Deddish MR, Day E: Value of periodic examinations in detecting cancer of the rectum and colon. Postgrad Med 27: 290-294, 1960.

36. Gilbertsen VA: Proctosigmoidoscopy and polypectomy in reducing the incidence of rectal cancer. Cancer 34 (3): suppl:936-9, 1974. [PUBMED Abstract]

37. Friedman GD, Collen MF, Fireman BH: Multiphasic Health Checkup Evaluation: a 16-year follow-up. J Chronic Dis 39 (6): 453-63, 1986. [PUBMED Abstract]

38. Selby JV, Friedman GD, Quesenberry CP Jr, et al.: A case-control study of screening sigmoidoscopy and mortality from colorectal cancer. N Engl J Med 326 (10): 653-7, 1992. [PUBMED Abstract]

39. Newcomb PA, Norfleet RG, Storer BE, et al.: Screening sigmoidoscopy and colorectal cancer mortality. J Natl Cancer Inst 84 (20): 1572-5, 1992. [PUBMED Abstract]

40. Slattery ML, Edwards SL, Ma KN, et al.: Colon cancer screening, lifestyle, and risk of colon cancer. Cancer Causes Control 11 (6): 555-63, 2000. [PUBMED Abstract]

41. Zheng S, Liu XY, Ding KF, et al.: Reduction of the incidence and mortality of rectal cancer by polypectomy: a prospective cohort study in Haining County. World J Gastroenterol 8 (3): 488-92, 2002. [PUBMED Abstract]

42. Winawer SJ, Fletcher RH, Miller L, et al.: Colorectal cancer screening: clinical guidelines and rationale. Gastroenterology 112 (2): 594-642, 1997. [PUBMED Abstract]

43. Vernon SW: Participation in colorectal cancer screening: a review. J Natl Cancer Inst 89 (19): 1406-22, 1997. [PUBMED Abstract]

44. Weissfeld JL, Ling BS, Schoen RE, et al.: Adherence to repeat screening flexible sigmoidoscopy in the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial. Cancer 94 (10): 2569-76, 2002. [PUBMED Abstract]

45. Weissfeld JL, Schoen RE, Pinsky PF, et al.: Flexible sigmoidoscopy in the PLCO cancer screening trial: results from the baseline screening examination of a randomized trial. J Natl Cancer Inst 97 (13): 989-97, 2005. [PUBMED Abstract]

46. Winawer S, Fletcher R, Rex D, et al.: Colorectal cancer screening and surveillance: clinical guidelines and rationale-Update based on new evidence. Gastroenterology 124 (2): 544-60, 2003. [PUBMED Abstract]

47. Smith RA, von Eschenbach AC, Wender R, et al.: American Cancer Society guidelines for the early detection of cancer: update of early detection guidelines for prostate, colorectal, and endometrial cancers. Also: update 2001--testing for early lung cancer detection. CA Cancer J Clin 51 (1): 38-75; quiz 77-80, 2001 Jan-Feb. [PUBMED Abstract]

48. Schoen RE, Pinsky PF, Weissfeld JL, et al.: Results of repeat sigmoidoscopy 3 years after a negative examination. JAMA 290 (1): 41-8, 2003. [PUBMED Abstract]

49. Doria-Rose VP, Levin TR, Selby JV, et al.: The incidence of colorectal cancer following a negative screening sigmoidoscopy: implications for screening interval. Gastroenterology 127 (3): 714-22, 2004. [PUBMED Abstract]

50. Lieberman DA, Weiss DG; Veterans Affairs Cooperative Study Group 380.: One-time screening for colorectal cancer with combined fecal occult-blood testing and examination of the distal colon. N Engl J Med 345 (8): 555-60, 2001. [PUBMED Abstract]

51. Gondal G, Grotmol T, Hofstad B, et al.: The Norwegian Colorectal Cancer Prevention (NORCCAP) screening study: baseline findings and implementations for clinical work-up in age groups 50-64 years. Scand J Gastroenterol 38 (6): 635-42, 2003. [PUBMED Abstract]

52. Winawer SJ, Stewart ET, Zauber AG, et al.: A comparison of colonoscopy and double-contrast barium enema for surveillance after polypectomy. National Polyp Study Work Group. N Engl J Med 342 (24): 1766-72, 2000. [PUBMED Abstract]

53. Lieberman DA, Weiss DG, Bond JH, et al.: Use of colonoscopy to screen asymptomatic adults for colorectal cancer. Veterans Affairs Cooperative Study Group 380. N Engl J Med 343 (3): 162-8,

2000. [PUBMED Abstract]

54. Imperiale TF, Wagner DR, Lin CY, et al.: Risk of advanced proximal neoplasms in asymptomatic adults according to the distal colorectal findings. N Engl J Med 343 (3): 169-74, 2000. [PUBMED Abstract]

55. Schoenfeld P, Cash B, Flood A, et al.: Colonoscopic screening of average-risk women for colorectal neoplasia. N Engl J Med 352 (20): 2061-8, 2005. [PUBMED Abstract]

56. Regula J, Rupinski M, Kraszewska E, et al.: Colonoscopy in colorectal-cancer screening for detection of advanced neoplasia. N Engl J Med 355 (18): 1863-72, 2006. [PUBMED Abstract]

57. Barclay RL, Vicari JJ, Doughty AS, et al.: Colonoscopic withdrawal times and adenoma detection during screening colonoscopy. N Engl J Med 355 (24): 2533-41, 2006. [PUBMED Abstract]

58. Ferrucci JT: Colon cancer screening with virtual colonoscopy: promise, polyps, politics. AJR Am J Roentgenol 177 (5): 975-88, 2001. [PUBMED Abstract]

59. Yee J, Akerkar GA, Hung RK, et al.: Colorectal neoplasia: performance characteristics of CT colonography for detection in 300 patients. Radiology 219 (3): 685-92, 2001. [PUBMED Abstract]

60. Miao YM, Amin Z, Healy J, et al.: A prospective single centre study comparing computed tomography pneumocolon against colonoscopy in the detection of colorectal neoplasms. Gut 47 (6): 832-7, 2000. [PUBMED Abstract]

61. Pickhardt PJ, Choi JR, Hwang I, et al.: Computed tomographic virtual colonoscopy to screen for colorectal neoplasia in asymptomatic adults. N Engl J Med 349 (23): 2191-200, 2003. [PUBMED Abstract]

62. Cotton PB, Durkalski VL, Pineau BC, et al.: Computed tomographic colonography (virtual colonoscopy): a multicenter comparison with standard colonoscopy for detection of colorectal neoplasia. JAMA 291 (14): 1713-9, 2004. [PUBMED Abstract]

63. Iannaccone R, Laghi A, Catalano C, et al.: Computed tomographic colonography without cathartic preparation for the detection of colorectal polyps. Gastroenterology 127 (5): 1300-11, 2004. [PUBMED Abstract]

64. McFarland EG, Zalis ME: CT colonography: progress toward colorectal evaluation without catharsis. Gastroenterology 127 (5): 1623-6, 2004. [PUBMED Abstract]

65. Edwards JT, Wood CJ, Mendelson RM, et al.: Extracolonic findings at virtual colonoscopy: implications for screening programs. Am J Gastroenterol 96 (10): 3009-12, 2001. [PUBMED Abstract]

66. Hellström M, Svensson MH, Lasson A: Extracolonic and incidental findings on CT colonography (virtual colonoscopy). AJR Am J Roentgenol 182 (3): 631-8, 2004. [PUBMED Abstract]

67. Gluecker TM, Johnson CD, Wilson LA, et al.: Extracolonic findings at CT colonography: evaluation

of prevalence and cost in a screening population. Gastroenterology 124 (4): 911-6, 2003. [PUBMED Abstract]

68. Mulhall BP, Veerappan GR, Jackson JL: Meta-analysis: computed tomographic colonography. Ann Intern Med 142 (8): 635-50, 2005. [PUBMED Abstract]

69. Herrinton LJ, Selby JV, Friedman GD, et al.: Case-control study of digital-rectal screening in relation to mortality from cancer of the distal rectum. Am J Epidemiol 142 (9): 961-4, 1995. [PUBMED Abstract]

70. Kinzler KW, Vogelstein B: Lessons from hereditary colorectal cancer. Cell 87 (2): 159-70, 1996. [PUBMED Abstract]

71. Dong SM, Traverso G, Johnson C, et al.: Detecting colorectal cancer in stool with the use of multiple genetic targets. J Natl Cancer Inst 93 (11): 858-65, 2001. [PUBMED Abstract]

72. Traverso G, Shuber A, Levin B, et al.: Detection of APC mutations in fecal DNA from patients with colorectal tumors. N Engl J Med 346 (5): 311-20, 2002. [PUBMED Abstract]

73. Traverso G, Shuber A, Olsson L, et al.: Detection of proximal colorectal cancers through analysis of faecal DNA. Lancet 359 (9304): 403-4, 2002. [PUBMED Abstract]

74. Ahlquist DA, Skoletsky JE, Boynton KA, et al.: Colorectal cancer screening by detection of altered human DNA in stool: feasibility of a multitarget assay panel. Gastroenterology 119 (5): 1219-27, 2000. [PUBMED Abstract]

75. Imperiale TF, Ransohoff DF, Itzkowitz SH, et al.: Fecal DNA versus fecal occult blood for colorectal-cancer screening in an average-risk population. N Engl J Med 351 (26): 2704-14, 2004. [PUBMED Abstract]

76. Woolf SH: A smarter strategy? Reflections on fecal DNA screening for colorectal cancer. N Engl J Med 351 (26): 2755-8, 2004. [PUBMED Abstract]

Changes to This Summary (09/13/2007)

The PDQ cancer information summaries are reviewed regularly and updated as new information becomes available. This section describes the latest changes made to this summary as of the date above.

Evidence of Benefit [10]

Added Newer FOBTs: Nonrandomized Controlled Trial Evidence [11] as a new subsection.

Added text [12] about a population-based, case-control study in Germany, 39%, 77%, and 64% of proximal, distal, and total CRCs were estimated to be preventable by colonoscopy.

Questions or Comments About This Summary

If you have questions or comments about this summary, please send them to Cancer.gov through the Web

site's Contact Form [13]. We can respond only to email messages written in English.

More Information

About PDQ

- PDQ® - NCI's Comprehensive Cancer Database [14].

  Full description of the NCI PDQ database.

Additional PDQ Summaries

- PDQ® Cancer Information Summaries: Adult Treatment [15]

  Treatment options for adult cancers.

- PDQ® Cancer Information Summaries: Pediatric Treatment [16]

  Treatment options for childhood cancers.

- PDQ® Cancer Information Summaries: Supportive Care [17]

  Side effects of cancer treatment, management of cancer-related complications and pain, and psychosocial concerns.

- PDQ® Cancer Information Summaries: Screening/Detection (Testing for Cancer) [18]

  Tests or procedures that detect specific types of cancer.

- PDQ® Cancer Information Summaries: Prevention [19]

  Risk factors and methods to increase chances of preventing specific types of cancer.

- PDQ® Cancer Information Summaries: Genetics [20]

  Genetics of specific cancers and inherited cancer syndromes, and ethical, legal, and social concerns.

- PDQ® Cancer Information Summaries: Complementary and Alternative Medicine [21]

  Information about complementary and alternative forms of treatment for patients with cancer.

Important:

This information is intended mainly for use by doctors and other health care professionals. If you have questions about this topic, you can ask your doctor, or call the Cancer Information Service at **1-800-4-CANCER (1-800-422-6237)**.

Table of Links

[1] http://cancer.gov/cancertopics/pdq/prevention/colorectal/HealthProfessional
[2] http://cancer.gov/cancertopics/pdq/treatment/colon/HealthProfessional
[3] http://cancer.gov/cancertopics/pdq/treatment/rectal/HealthProfessional
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Standards for Gastroenterologists for Performing and Interpreting Diagnostic Computed Tomographic Colonography

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Executive Summary

Prominent among a number of new techniques with which to image the colon, computed tomographic (CT) colonography is extremely attractive because it is noninvasive and also relatively simple for patients to undergo. As the technology evolves, it is important that gastroenterologists not only understand the multiple issues surrounding CT colonography but also that they be able to interpret this examination.[1] The American Gastroenterological Association (AGA) Institute's Governing Board convened the CT Colonography Task Force to develop training standards for gastroenterologists for CT colonography. These standards are intended to outline the basic requirements that board-certified gastroenterologists should meet to be involved in and/or perform CT colonography. All recommendations are based on the literature available at the time this manuscript was developed.

A wide range of sensitivities have been reported for CT colonography; therefore, the current use of CT colonography in clinical practice is controversial. Several studies have evaluated the use of CT colonography after failed colonoscopy; its sensitivity for detecting important lesions is comparable with or better than results with air contrast barium enema (ACBE). CT colonography appears to also be useful for evaluation of the colon proximal to an obstructing lesion. Minimal data are available regarding the use of CT colonography as a screening test in patients with contraindications to colonoscopy or who refuse other screening options. The results of studies using CT colonography as a colorectal cancer (CRC) screening test suggest that this is an area requiring further study. The use of CT colonography for CRC screening is currently controversial and this test has not yet been endorsed as a primary CRC screening tool in asymptomatic, normal-risk adults by any multidisciplinary group involved in CRC screening guideline development.

CT colonography has few contraindications; however, it should not be performed in patients in whom perforation is a risk and should probably not be performed immediately after failed colonoscopy in patients who had polyps removed or large biopsy specimens taken during colonoscopy because of the risk of perforation from colonic insufflation. Specific clinical circumstances may also exist in which endoscopic examination is preferred to CT colonography (such as patients with known inflammatory bowel disease, high-risk symptoms, and others). Overall, the Task Force finds that CT colonography is appropriate in certain circumstances and has developed the following recommendations to guide gastroenterologists who are interested in performing CT colonography.

CT scanning should be performed by American Registry of Radiologic Technologists-certified radiologic technologists. The extent of training for gastroenterologists to read accurately CT colonography has not been fully defined. However, research shows that response to training is unpredictable, and the "learning curve" for CT colonography interpretation will vary widely among observers. Available literature suggests that review of at least 75 endoscopically confirmed cases is appropriate as a requirement for minimal competence in detecting and characterizing colorectal neoplasia detected by CT colonography. Subsequently, interpretation under the supervised guidance of a qualified physician mentor is required. To maintain clinical expertise in CT colonography after formalized training, physicians should supervise and interpret a minimum number of cases per year, in addition to participating in continuing medical education activities, and update them relating to advances in the field.

Most bowel preparative regimens employ a cathartic agent, the selection of which will depend on patient

Abbreviations used in this paper: ACBE, air contrast barium enema; CRC, colorectal cancer; CT, computed tomography.

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factors as well as physician preferences. Fecal and fluid tagging may permit identification of submerged polyps and reduce false-positive examinations. CT colonography performed without a bowel purge is an area of great promise but cannot currently be recommended because no large clinical studies have verified its performance in a large cohort. Colonic insufflation with automated insufflators results in improved colonic distention compared with manual insufflation.

High-resolution CT is performed in the supine and prone positions following review of an initial CT scout. CT colonography evaluation involves the following 2 steps: first, a primary search for suspicious colonic lesions and, second, lesion characterization. The primary search can be achieved using either a primary 2-dimensional (2D) search or a primary 3-dimensional (3D) search; optimal performance likely involves both search methods. Lesion characterization includes determination of lesion density and lesion mobility.

Reading

All intracolonic findings should be examined, and any segment not adequately evaluated should be documented. All large masses and lesions that compromise luminal caliber should be communicated. The size and location of colorectal lesions should be reported. Extracolonic findings are common, but the majority of these lesions are not clinically significant and do not require follow-up. Characterizing these extracolonic lesions requires expertise in recognizing abnormalities of the lungs, the solid organs, the retroperitoneum, and the extracolonic gastrointestinal tract. A radiologist should review the extracolonic portion of the study.

Reporting

A standardized CT colonography report should encompass elements of preprocedure documentation, patient demographics, indications, technical description, findings, clinical assessment, and recommendations (plan) for follow-up. Reporting by polyp size is controversial. General agreement exists that all polyps $\geq$10 mm should be reported. However, full consensus relating to the reporting or management of subcentimeter polyps discovered at CT colonography has not been reached. The referral of patients to endoscopy for diminutive lesions (when CT colonography specificity is low) could lead to inappropriate referrals to colonoscopy. Moreover, current CT colonography acquisition parameters are tailored to the detection of polyps 6 to 10 mm in diameter. Based on these considerations, it is recommended that all polyps 6 mm or larger should be reported. Controversy exists for small lesions; these should be reported when reader confidence is very high. Extracolonic findings should be reported.

A comprehensive technical and professional quality control program is necessary. Technical quality control should encompass both the CT scanner and the CT colonography workstation. Professional quality assessment monitors outcomes within a practice for internal quality assessment purposes. Such measures will alert physicians that changes may need to be made in patient educational materials, patient preparation regimens, or interpretation techniques. Retrospective, sporadic review of CT colonography parameters and reports can also ensure that appropriate technique and practice patterns are being followed. Standardized practices followed by all physicians and allied health personnel within a practice can also improve patient safety.

Regulatory Issues

Federal anti-kickback laws and Stark statutes influence who can perform CT colonography as well as the subject of split interpretation (a situation in which one physician interprets intracolonic images and another performs the extracolonic images). Both performing and interpreting CT colonography constitute "designated health services" and are therefore subject to Stark statutory requirements regarding referrals and billing for split interpretation. Compensation arrangements in a situation in which there is dual interpretation are potentially complicated but should not exclude any group from reading CT colonography. A personal services and management agreement ("safe harbor") is a potentially applicable compensation arrangement between the gastroenterologist and the radiologist in a split interpretation scheme.

Key Executive Summary Recommendations

The key Task Force recommendations related to the basic requirements that board-certified gastroenterologists should meet to be involved in and/or perform CT colonography are summarized below. A complete list of recommendations is included in the full Task Force report.

- CT colonography is effective for evaluation of the colon proximal to an obstructing lesion.
- CT colonography is indicated for adults with failed colonoscopy in whom evaluation of the colon is deemed necessary.
- Minimal data are available regarding the use of CT colonography as a CRC screening test in patients with contraindications to colonoscopy or those who refuse other screening options. CT colonography may be considered in patients unwilling to undergo other primary screening modalities.
- Based on currently available data, CT colonography is not endorsed as a primary screening modality for CRC in asymptomatic adults.
- Training for CT colonography interpretation should

include review and interpretation of at least 75 cases with endoscopic correlation.

- Subsequent to formal training, the gastroenterologist should participate in a mentored CT colonography preceptorship lasting 4 to 6 weeks, occurring within 6 months of the initial training, with the candidate physically present and involved in the interpretation of at least 25–50 additional cases.
- It is expected that those performing CT colonography will undertake ongoing training and self-assessment including attending formal continuing medical education accredited courses in CT colonography.
- Gastroenterologists should work collaboratively with board-certified radiologists to review the extracolonic portion of the CT colonography examination.
- Any polyp ≥6 mm in size (ie, widest diameter) should be reported and the patient referred for consideration of endoscopic polypectomy.
- Patients with 3 or more polyps of any size in the setting of high diagnostic confidence should be referred for consideration of endoscopic polypectomy.
- The appropriate clinical management of patients with 1 or 2 lesions no greater than 5 mm in diameter is unknown. In the absence of data, the follow-up interval recommended for these patients should be based on individual characteristics of the patient and the procedure.
- Gastroenterologists considering offering CT colonography should consult with their health care counsel regarding compliance with state and local regulations.

Full Task Force Review and Recommendations

Introduction

ACBE and colonoscopy have been used to image the colon for many years. Recently, a number of new techniques with which to image the colon have been introduced.[2] Prominent among these is CT colonography (also CTC, CT colography, or "virtual colonoscopy"). CT colonography is a high spatial resolution, low-dose CT examination of the abdomen and pelvis performed following colonic insufflation. CT data sets are reviewed on a computer workstation that generates multidimensional images of the colon. CT colonography is extremely attractive because it is noninvasive and also (relatively) simple for patients to undergo.

As of the spring of 2006, one third of the membership of the American Gastroenterological Association indicated they were either already involved in some way with CT colonography or were interested in learning the technique in the future. Given the interest, and acknowledging the lack of training standards and guidance for gastroenterologists in this area, the American Gastroenterological Association Executive Committee convened the CT Colonography Task Force to develop minimum training standards for gastroenterologists for CT colonography.

Because of their subspecialized training, gastroenterologists are experts in CRC screening and colorectal disease. Gastroenterologists should be able to translate their knowledge of the endoscopic appearance of colorectal disease to CT colonography, following formalized training in the CT physics, use of intravenous contrast, CT colonography interpretation and image manipulation, and CT colonography performance characteristics. These standards are intended to outline the basic requirements that board-certified gastroenterologists should meet to be involved in and/or perform CT colonography.

Current Status of CT Colonography

Investigation of CT colonography accuracy has been underway since its introduction. CT colonography sensitivity has been studied extensively,[3–11] with the earliest reports involving small populations at high risk for colorectal pathology and using primarily single-row scanners (see Van Dam et al[12] for review). The per-polyp sensitivity of CT colonography compared with colonoscopy was excellent for larger lesions (some reports stated up to 100%) but was poor for smaller lesions (11%–55% sensitivity). These studies were extremely heterogeneous, varying in terms of patient cohorts, technical methodology, and training of CT colonographers.

Subsequently, further studies demonstrated improved detection sensitivity for polypoid lesions but continued to reveal wide variation in results. In general, the per-polyp sensitivities for lesions based on polyp size were greatest for larger lesions and were in the following ranges: <5 mm (30%–60%), 6–9 mm (45%–85%), and ≥10 mm (60%–95%). The specificity of CT colonography varied as well but was generally in the 90%–95% range. Most recently, 2 larger multicenter studies demonstrated that CT colonography was significantly less sensitive than colonoscopy,[3,4] whereas a third reported that it was as sensitive as colonoscopy for detection of lesions ≥10 mm.[5]

A number of variables appear to contribute to the wide range of sensitivities reported for CT colonography. First and perhaps most importantly, as technology has evolved, so has the approach to CT colonography patient preparation and image acquisition. Multidetector CT scanners permit faster scanning with fewer motion artifacts while improving spatial resolution, and automated insufflators improve colonic inflation. Software platforms used to evaluate CT colonography images have also evolved, permitting greater interactivity and improved 3D visualization techniques for surveying the colonic lumen.

Additionally, bowel preparation methods have been variable, and some studies have used oral contrast, whereas others have not. A further critical variable is the cohort of individuals examined. Some studies have examined patients at high risk for colon abnormalities, and others have examined cohorts at low risk. Most studies have examined highly variable cohorts. Finally, the method in which it was ascertained that lesions detected by CT colonography were accurately assessed has varied as well. Colonoscopy has typically been used as the "gold standard"; however, colonoscopy does not detect all lesions, including large polyps.[13] Thus, its use as a "gold standard" may not be appropriate. One study reported use of a "consensus" view of the colon based on the results of 3 different colon imaging tests as the reference standard,[3] an approach likely to be more appropriate than simple use of colonoscopy results.

Additionally, new modifications in software such as novel display techniques, including so called "virtual dissection,"[14] validated computer-aided detection systems, and more are on the horizon.[15] Computer-aided detection systems recognize colorectal neoplasia by means of sophisticated thresholding followed by mathematical rule-based testing on the basis of feature values.[16,17] Although this technique appears to hold great promise, and will likely be readily integrated into reading schemes,[18] many issues remain to be resolved.

Considerable effort has also been directed at developing CT colonography with minimal preparation.[19–24] Performance of CT colonography without a cathartic preparation, if proven to be highly sensitive and safe, could revolutionize the entire field.

It is essential that clinicians realize that this area is rapidly evolving and will continue to evolve for the next several years. Several large studies are currently under way that will further impact the practice of colon imaging.

Current Indications for CT Colonography

The current utility of CT colonography is controversial. Some believe that with a sensitivity level generally below that for colonoscopy, implementation should be limited. Others believe that it is ready to be widely implemented. Indications for CT colonography are highlighted below.

Failed Colonoscopy

Incomplete colonoscopic examination occurs in 2%–5% of colonoscopic examinations, usually secondary to patient discomfort or uncooperativeness, anatomic irregularities (eg, tortuosity, strictures, excessive looping), obscuring cancers, or inadequate colon preparation.[25] ACBE has traditionally been the test of choice for patients in whom colonoscopy could not be completed. However, ACBE may be difficult to perform immediately after a failed colonoscopy, and barium coating of the colon wall is sometimes suboptimal after certain colon preparations, usually requiring the patient to undergo an ACBE-specific bowel preparation. Several studies have evaluated the use of CT colonography after failed colonoscopy. In one study, CT colonography and ACBE had comparable results in 10 patients after incomplete colonoscopy.[26] In another study, CT colonography was performed within 2 hours after incomplete colonoscopy in 40 patients, all of whom either had lower gastrointestinal symptoms or who were at increased risk of CRC.[27] Among the 26 patients who underwent both CT colonography and ACBE, CT colonography was better tolerated ($P < .001$), and CT colonography was judged to adequately reveal 96% of colonic segments compared with 91% for ACBE. Multiple intracolonic abnormalities were described in this at-risk population.

Evaluation of Colon Proximal to an Obstructing Lesion

Current screening guidelines recommend examination of the colon proximal to a CRC lesion because synchronous neoplastic lesions are found in 5%–8% of patients diagnosed with CRC.[28,29] One study evaluated 29 patients without acute bowel obstruction in which the colonoscope could not be advanced proximal to the obstructing lesion.[30] In this trial, findings on CT colonography were compared with findings from preoperative ACBE and/or colonoscopy. CT colonography identified 100% of the occlusive CRC as well as 24 proximal colonic polyps and 2 synchronous proximal adenocarcinomas. In the 4 patients who had preoperative ACBE, ACBE failed to evaluate adequately the proximal colon in any patient, whereas CT colonography adequately examined the proximal colon in all of these patients, one of whom had a synchronous CRC. In another study of 19 patients with distal, occluding CRC,[31] CT colonography identified all 19 distal lesions as well as 22 lesions proximal to the obstruction, including 2 adenocarcinomas. ACBE was attempted but was unsuccessful in 5 patients, whereas CT colonography adequately demonstrated the proximal colon in all 5 of these patients.

Colonic strictures because of radiation therapy, previous surgery, inflammatory bowel disease, or nonsteroidal anti-inflammatory drugs can also prevent complete colonoscopy. CT colonography has been shown to permit adequate visualization of the proximal colon in these patients.[32] To date, no trials have specifically examined the role of CT colonography in a population of patients with colonic strictures because of a single etiology, but, in one prospective study[32] of patients with a history of abdominopelvic surgery and/or radiation (41 patients) and controls (20 patients), CT colonography was judged to be successful in all patients. Although clinical outcomes, such as CT colonography sensitivity were not

reported, these data suggest that CT colonography is safe and feasible in this population.

CRC Screening in Patients With Contraindications to Colonoscopy or Who Refuse Other Screening Options

Minimal data are available regarding the use of CT colonography as a screening test in patients with contraindications to colonoscopy (eg, coagulopathy, intolerance to sedation) or who refuse other screening options. However, this is a critical area in which CT colonography may be beneficial. Elderly patients may be another population that could benefit from CT colonography because numerous studies have documented high sensitivity of CT colonography for cancer and the incidence of CRC increases with age. CRC screening of the elderly population with CT colonography is subject to many of the same concerns and criticisms as screening this population with colonoscopy. A recent analysis of screening colonoscopy in the elderly population found that the gain in life expectancy was only 15% of that observed in a younger population.[33] However, a gain in life expectancy is still derived from CRC screening in this population, so the authors recommended that the decision to screen patients of age ≥80 years be individualized.

CRC Screening of Asymptomatic, Normal-Risk Adults

Multiple trials have examined the accuracy of CT colonography for the identification of CRC and polyps. Most of the early efforts investigated the role of CT colonography in patients who were at greater than average risk for the development of CRC or who had symptoms referable to the lower gastrointestinal tract.[34–36] Other studies examining CT colonography accuracy for detecting CRC and colon polyps in screening populations have been published.[5,6,37–39] Taken as a whole, the body of literature examining CT colonography as a CRC screening test demonstrates significant variability (see Current Status of CT Colonography, above). A recent meta-analysis of 33 studies comparing CT colonography screening to a gold standard (colonoscopy or surgery) concluded that issues such as patient selection, examiner training and experience, scanner collimation and type, and mode of imaging are likely contributors to the heterogeneity observed in these trials.[40] The heterogeneity of studies in this meta-analysis was felt to preclude conclusions about use of CT colonography as a primary screening modality.

The largest trial of CT colonography as a CRC screening test in average-risk patients was conducted with 1233 patients at a number of military tertiary care hospitals.[5] Sensitivity of CT colonography for adenomas ≥1 cm was 94%, compared with colonoscopy as the gold standard. This trial utilized experienced CT colonography interpreters, fecal and fluid tagging with subsequent digital subtraction of retained stool and fluid in the colon, and relied on a primary 3D interpretation of CT colonography images, all techniques that distinguished it from previous, as well as subsequent, studies. Whether or not these factors were critical in the encouraging results observed in this trial remains controversial. Currently, investigators from the military hospital that contributed the majority of the patients for the study cited above are performing a 3000 person study designed to explore further the use of CT colonography as a CRC screening test.[39] Preliminary data from this trial have been encouraging, demonstrating diagnostic equivalence of CT colonography with colonoscopy for adenomas ≥6 mm in size.[39]

CT colonography has not yet been endorsed as a primary CRC screening test by any multidisciplinary group involved in CRC screening guideline development.[29,41,42] Additionally, Medicare does not pay for screening tests in the absence of symptoms. For that reason, the majority of Medicare contractors do not cover CT colonography for CRC screening in asymptomatic patients. It is also not a covered benefit offered by most private insurance companies, although pilot programs have produced promising results.[43]

Contraindications

CT colonography has few contraindications, however, it should not be performed in patients for whom perforation is a concern. In addition, CT colonography should probably not be performed immediately after failed colonoscopy in patients who had polyps removed or large biopsy specimens taken because of the possible risk of perforation resulting from the required colonic insufflation with CT colonography. Specific clinical circumstances exist in which endoscopic examination is preferred to CT colonography. These include, but are not limited to, situations in which the pretest probability of identifying colonic abnormalities is increased, such as patients with symptoms of organic gastrointestinal disease, patients with familial colon cancer syndromes, or patients with inflammatory bowel disease in whom colonic sampling for dysplasia is recommended.

Task Force Recommendations

- CT colonography is effective for evaluation of the colon proximal to an obstructing lesion.
- CT colonography is indicated for adults with failed colonoscopy in whom evaluation of the colon is deemed necessary.
- Minimal data are available regarding the use of CT colonography as a screening test in patients with contraindications to colonoscopy or who refuse other screening options. CT colonography may be considered in patients unwilling to undergo colonoscopy as a primary screening modality.
- CT colonography should not be performed immedi-

ately after failed colonoscopy in patients who had polyps removed or large biopsy specimens taken during the failed colonoscopy.

- CT colonography is not indicated in patients with high-risk disease symptoms (eg, inflammatory bowel disease, hematochezia) and situations in which the pretest probability of identification of colonic abnormality is increased.
- Based on the data currently available, CT colonography is not endorsed as a primary screening modality for CRC in asymptomatic adults.
- Additional studies comparing CT colonography and other primary screening modalities are required.

Qualifications and Training of Personnel

CT Scanning

CT scanning should be performed by American Registry of Radiologic Technologists-certified radiologic technologists. Prior to CT acquisition, adequate colonic inflation is confirmed using a CT scout. Suboptimal colonic distention can result in falsely negative CT examinations,[44] so personnel performing CT colonography need to be facile with equipment and techniques to ensure adequate distention. Therefore, a program to ensure technologist expertise in review of CT scout images is required.

Skill and Training to Read CT Colonography

Despite the intensive study and evolution that CT colonography has undergone over the last decade, the extent of training for gastroenterologists to read accurately CT colonography has not been defined. The American College of Radiology practice guidelines[45] for performing and interpreting diagnostic CT requires licensed medical practitioners who have a thorough understanding of the indications for CT as well as a familiarity with the basic principles and limitations of the technology. Individuals performing CT colonography should have a thorough understanding of CT technology and instrumentation as well as radiation safety. With respect to CT colonography in particular, the American College of Radiology[46] recommends that the supervising and interpreting physicians should have reviewed at least 50 cases in one or more of the following formats: (1) formal hands-on interactive training on CT colonography interpretation, (2) supervision with a CT colonography-trained physician(s) acting as a double reader, and (3) correlation of CT colonography and endoscopy findings in patients who undergo both procedures. Furthermore, the current Gastroenterology Core Curriculum suggests that trainees "Gain familiarity with the detection of neoplasms of the colon during the performance of CT colonography and other similar techniques."[47]

A number of studies have examined the variability in the "learning curve" associated with interpretation of CT colonography findings. In one, with 2 blinded teams made up of a radiologist and gastroenterologist,[48] it was found that increasing experience (after reading 25 cases) led to enhanced specificity and reduced interpretation times. In a study examining reader training at 25, 50, 75, and 96 case intervals, sensitivity improved after reading 50 cases, whereas optimal sensitivity (92% for target lesions) was achieved after interpreting 75 cases.[49] Another study reported similar findings at the 75-case threshold,[49] with this study using 2 readers with limited prior experience in reading CT colonography. The performance of nonradiologists (medical students and radiologic technologists) after training using a teaching file of 50 cases followed by blind interpretation of 50 cases with colonoscopic correlation (30 positive, 20 negative) was similar to a separate cohort of radiologists learning CT colonography; interestingly, the performance of nonradiologists improved further following reading of another 100 cases.[50]

Response to training is unpredictable. In one study, 3 radiologists (gastrointestinal radiology consultant, research fellow, and trainee) with no prior experience in CT colonography were tested on 100 cases.[51] Feedback and training were given after the first 50 cases, and performance and reporting times were compared for these and then 50 subsequent data sets. Prior experience of gastrointestinal radiology enhanced the ability to read CT colonography; however, competency could not be assumed after direct training with the database of 50 cases. In another study, inexperienced CT colonography readers ($<$50 cases read) who completed a CT colonography training module performed better than experienced CT colonography readers with a sensitivity of 70% vs 47%, respectively, in detecting lesions $\geq$10 mm.[3] In a study examining performance variability among 6 readers (4 residents, 2 subspecialty gastrointestinal radiologists) without prior CT colonography training in reading (20 cases including 32 polyps), untrained reader sensitivity was low, with marked individual variation; the majority of missed polyps were due to failure of detection (82%–95%).[52] Based on these observations, the learning curve for CT colonography interpretation will vary widely among observers.

The American College of Cardiology and the American Heart Association recently established criteria for clinical competence in interpreting computed tomography and magnetic resonance imaging studies of the heart, based on physician training and the cognitive skills required for each type of examination.[53] Training for each level of clinical competence is based on the cognitive skills required for each scope of practice. Table 1 summarizes the cognitive skills required for physician competence at CT colonography.

Table 1. Cognitive Skills Required for Physician Competence in CT Colonography

Knowledge relating to the colon
• Knowledge of colon, rectal, appendiceal, and ileal anatomy
• Knowledge of colorectal diseases and colon cancer screening recommendations and alternatives
Knowledge relating to CT colonography data acquisition and interpretation of colonic findings
• Knowledge of basic CT physics and CT parameters/acquisition techniques that affect radiation exposure
• Familiarity with colonic insufflation devices
• Knowledge of indications for iodinated intravenous contrast, as well as knowledge of contraindications and treatment of adverse reactions
• Knowledge of spectrum of bowel purgation and cleansing regimens used at CT colonography
• Knowledge of CT colonography interpretation technique
• Knowledge of the varied appearance of colorectal neoplasia at CT colonography
• Knowledge of the performance characteristics of CT colonography for polyps of different sizes and histologies
• Knowledge of the appearance of colonic, rectal, ileal, appendiceal disease at CT
• Knowledge and familiarity with a dedicated CT colonography workstation, including the ability to compare supine and prone images, generate 2D and 3D endoluminal images, and examine CT attenuation
Knowledge relating to the identification and workup of extracolonic disease
• Knowledge of the appearance of extracolonic mass lesions within the abdomen and pelvis at CT
• Understanding of how low-dose, unenhanced CT images affect the ability of CT to display extracolonic structures and findings
• Understanding of appropriate medical workup following the detection of potentially important extracolonic findings

Qualifications for Interpretation of CT Colonography Data Sets

As discussed previously, available literature suggests that review of at least 75 endoscopically confirmed cases is necessary for minimal competence in detecting and characterizing colorectal neoplasia at CT colonography. Because formalized training improves, but does not ensure, adequate performance, CT colonography interpretation under the supervised guidance of a qualified physician mentor is required. Candidates should participate in mentored interpretation during this training period. During this preceptorship, gastroenterologists would be expected to hone the ability to track the colon using CT colonography workstations (a known difficulty for nonradiologists[50]), gain experience in performing quality assessment prior to patient dismissal, become familiar with the application of problem-solving salvage techniques used to improve examination quality, and, of course, refine their ability to detect and characterize colonic lesions. Routine use of a validated computer-aided detection system may also prove helpful[18,54,55] but cannot be recommended without further data.

Continued Competence in CT Colonography

Ongoing practical experience with the acquisition and interpretation of CT colonography studies is required to maintain clinical competence. Mammography has similar requirements. To maintain clinical expertise in CT colonography after formalized training, physicians should supervise and interpret a minimum number of cases per year, in addition to participating in continuing medical education activities, and update them relating to advances in the field.

Task Force Recommendations

- Gastroenterologists performing and interpreting CT colonography should have a thorough understanding of the indications and the principles and limitations of CT colonography technology.
- Formalized training of gastroenterologists for CT colonography interpretation is mandatory.
- Training for CT colonography interpretation should address cognitive skills required to perform all aspects of the CT colonography examination (Table 1).
- Training should include review and interpretation of at least 75 cases with endoscopic correlation.
- Subsequent to formal training, the gastroenterologist should participate in a mentored CT colonography preceptorship lasting 4 to 6 weeks, occurring within 6 months of the initial training, with the candidate physically present and involved in the interpretation of at least 25–50 additional cases.

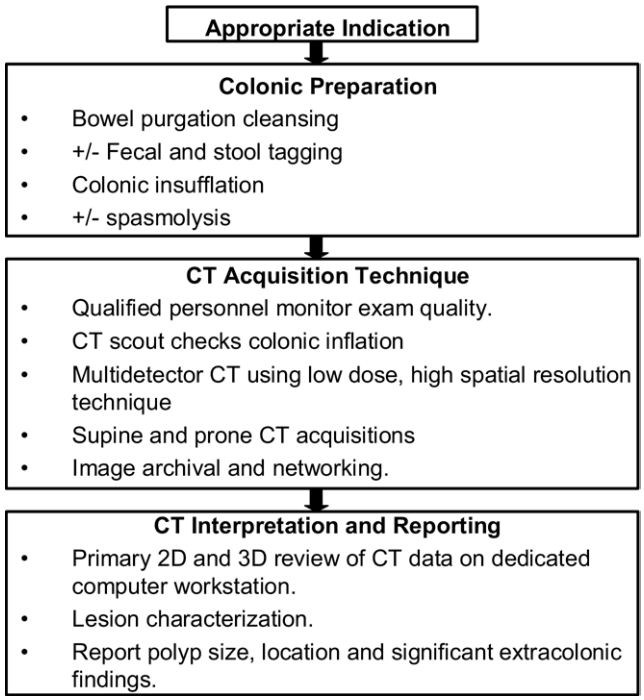

Figure 1. CT colonography care map.

- It is expected that there will be ongoing training and self-assessment including attending formal continuing medical education-accredited courses in CT colonography.
- CT colonography training should focus heavily on detection technique.

Examination and Equipment Specifications

The spectrum of CT colonography practice may vary widely depending on the clinical indication and available equipment, but adherence to recommended standards for all portions of the examination are required to achieve reproducible results (Figure 1).

Colonic Preparation

Most regimens employ a cathartic agent in addition to a colonic stimulant (usually bisacodyl tablets or suppositories). Polyethylene glycol electrolyte solution is a nonabsorbable, osmotically balanced preparation that is safe and results in little fluid shifting during administration and is commonly used prior to CT colonography and colonoscopy. Oral sodium phosphate-based agents are easier to ingest for many patients, because of the smaller volume that must be consumed, but can result in electrolyte shifts when doses exceeding 45 mL daily are employed.[56] Magnesium citrate is a milder saline cathartic preparation, which performs similarly to polyethylene glycol for CT colonography when combined with fecal tagging agents.[57] Polyethylene glycol results in increased fluid within the colon compared with oral phosphasoda,[58] but this generally does not cause diagnostic problems if the patient is scanned in 2 positions to permit redistribution of colonic fluid. The selection of a cathartic agent will depend on patient factors as well as physician preferences; indeed, current preparative regimens for CT colonography are not well tolerated.[59] Patient factors include underlying conditions that lead to contraindications for electrolyte shifts, fluid shifts, or phosphate ingestion.

Tagging of colonic fluid and stool can be achieved with oral contrast agents prior to CT examination. Fecal and fluid tagging may permit identification of submerged polyps and reduce false-positive examinations because of residual stool.[60] Use of fecal and fluid tagging is not mandatory if the patient is adequately cleansed with cathartics and scanned in 2 positions, because both fluid and stool generally move with repositioning,[10] and is impractical when CT colonography is performed following incomplete endoscopy.[27,61] Stool tagging is generally achieved with ingestion of a barium suspension; fluid tagging is performed using an iodinated oral contrast agent. Compliance with fecal and fluid tagging regimens can be challenging for some patients (because of understanding or availability of the tagging agents). CT colonography performed without bowel purgation cleansing is a promising extension of the CT colonography technique[19–24] but cannot currently be recommended because no large clinical studies have documented its performance in an asymptomatic patient population.

Colonic insufflation is performed prior to CT acquisition using air or carbon dioxide, which may reduce postprocedure cramping.[62] Glucagon, a spasmolytic agent, does not increase colonic distention but may improve patient comfort.[63] Colonic insufflation with automated insufflators results in improved colonic distention compared with manual insufflation.[64] Automatic insufflators may also be safer because of preset ramped flow rates and automatic venting at predetermined intracolonic pressures.[65]

CT Acquisition Technique

Following review of an initial CT scout, high-resolution CT is performed in the supine and prone positions. Scanning the patient in 2 positions is mandatory, to permit redistribution of colonic fluid and air, and improves the detection of colonic polyps compared with a single position.[10,66]

The ability of CT colonography to detect colorectal polyps is in part dependent on CT acquisition parameters including slice thickness. Slice thickness should be chosen to be at least half of the target polyp size to minimize partial volume averaging with adjacent air. Multislice CT scanners have several advantages over single slice helical scanners for CT colonography. Faster tube rotation times and an increased number of detectors permit faster table speeds so that a patient can be scanned quicker. Faster scanning is important because the patient is holding his/her breath and may be experiencing some discomfort as the colon is maximally inflated. The use of multidetector CT consequently results in better colonic distention and fewer respiratory artifacts, compared with single slice helical CT.[67] For these reasons, CT colonography should be performed on multidetector scanners with 4 or more detectors. Additionally, most multislice CT scanners are equipped with automatic exposure control, which varies the x-ray tube current over the body region (as the patient travels through the scanner) and projection angle, and results in significant dose savings for average-sized patients.[68,69] Automatic exposure control may increase the dose for obese patients, as it normalizes noise across the imaged volume, but this dose increase may be important to maintain image quality in the bony pelvis in such patients. Although submillimeter slice thicknesses are now possible with 64-slice CT systems, utilization of such slice thicknesses results in data sets of thousands of images, increases image noise, and will result in increased radiation dose if noise is held constant. Numerous phantom experiments have demonstrated that polyps 6 mm or greater in size can be detected using slice thicknesses of 3 mm or less, with

narrower slice thicknesses potentially increasing lesion conspicuity.[70–72] Several large patient studies using 2.5- or 3-mm slice thickness have demonstrated acceptable performance for detecting polyps 6–9 mm in size.[5,9,73]

Unlike routine abdominal CT, which identifies solid organ abnormalities using differences in x-ray attenuation between soft tissue structures, CT colonography identifies colonic polyps and cancers by exploiting the attenuation difference between these soft tissue lesions and intracolonic air. The resulting attenuation gradient is much greater, permitting CT colonography examinations to be performed at much lower doses. Scanning at lower dose (ie, lower milliampere settings, higher pitch) increases image noise and complicates visualization of extracolonic structures but does not compromise the detection of colorectal polyps and cancers 5 mm or greater in size.[71,74–77] The radiation dose for CT colonography examinations using supine and prone acquisitions in published CT colonography protocols averages 8 mSv,[75] compared with the barium enema, which has an estimated effective dose of 4.0 mSv in males and 8.8 mSv in females.[78] The tube current used to achieve doses similar to barium enema varies depending on scanner model and other acquisition parameters but should be within this range for average-sized patients for routine CT colonography examinations. The American College of Radiology practice guidelines for CT colonography recommend a kVp of 120 kV and a tube current of <100 mAs for routine CT colonography examinations in adult patients.[46] The risk of radiation exposure to the public, based on typical CT acquisition parameters and extrapolated to cancer risk estimated for atomic bomb survivors of all ages who had whole body exposures of a mean of 20 mSv, appeared to be low.[79] Even with these assumptions (because CT colonography involved only older patients with diminished risk for an induced cancer and scanning of the abdomen and pelvis only), it was concluded that "the benefit-risk ratio is large for CT colonography." When characterization of solid organs is necessary (eg, to evaluate a potentially significant extracolonic finding or to stage an obstructing colon cancer), intravenous contrast with normal dose settings should be employed. Intravenous contrast may also be used to help allow better characterization of polyps (eg, to help distinguish polyp from stool, or in the setting of excess colonic fluid).[80] In these circumstances, normal dose settings are also appropriate so that the attenuation of colonic lesions can be accurately assessed.

Prior to patient dismissal, CT data sets should be reviewed by a trained technologist or physician to ensure complete imaging of the colorectum and adequate visualization of colonic segments. Repeat scanning after reinflation, changes in patient position, or intravenous contrast may be required if colonic segments are inadequately visualized because of collapse or excess fluid.[46,80] CT images should be sent to a dedicated CT workstation for interpretation as well as archived as part of the medical record for future comparison purposes.

CT Interpretation

CT colonography evaluation can be divided into the following 2 steps: (1) a primary search for suspicious colonic lesions and (2) lesion characterization. The primary search can be achieved using either an initial 2D search strategy, in which enlarged 2D images are evaluated sequentially from rectum to cecum,[36,81,82] or a primary 3D search, in which the endoluminal surface of the colon is reviewed.[83] Performing a primary 3D search in addition to a primary 2D search may increase sensitivity by approximately 10%[4] but requires additional interpretation time.[84] Primary 3D search has been cited as a reason for the high sensitivity achieved in some studies,[5] but smaller studies employing primary 2D search have also achieved similar results.[9,74] Flat lesions, which appear as cigar-shaped, plaque-like, focal regions of soft tissue attenuation, are best seen using 2D images.[85] Given the advantage of both primary 2D and 3D search, optimal performance likely involves both search methods. Lesion morphology is assessed by correlation of 2D and 3D images to distinguish polyps from folds. Lesion density is determined by visual interrogation of intralesional attenuation (to differentiate stool from neoplasia or lipoma). Lesion mobility is judged by comparison of lesion position on supine and prone images. When a polyp or cancer is identified, it should be measured on 2D images with lung window settings or using 3D endoluminal views.[86,87] Adequate CT colonography workstations permit the viewing of enlarged 2D images in multiple planes, 3D endoluminal navigation and interrogation, as well as simultaneous viewing of 2D and 3D images, simultaneous viewing of supine and prone images, and variation of window/level settings and field of view size to examine intralesional attenuation and the extracolonic tissues.[46]

Task Force Recommendations

- The bowel purgative method should be tailored to the patient and local endoscopy practice. Use of stool and fluid tagging agents is preferred but not mandatory.
- Dedicated personnel should be trained in manual and automated insufflation techniques. Automated insufflation is preferred but not mandatory.
- A CT scout should be performed prior to scanning to confirm adequate insufflation. Supine and prone CT acquisitions should be performed. Trained personnel should review 2D images of the colorectum prior to patient dismissal to ensure adequate visualization of all colonic segments.
- CT colonography should be performed using multi-

detector CT (minimum 4 detector) using protocols with high spatial resolution (ie, ≤3-mm slice thickness), low-dose (<100 mAs) technique. If intravenous contrast is needed, routine dose settings (>100 mAs) should be used.

- Computer workstations for dedicated CT colonography interpretation should permit comparison of supine and prone data sets, primary 2D and primary 3D visualization of the colonic lumen, correlation of 2D and 3D images, and 2D evaluation in multiple planes using a variety of window settings.
- CT colonography images should be archived for later comparison.
- Primary 2D or primary 3D review of the endoluminal surface of the colorectum is required. Combined primary 2D and primary 3D review is recommended but not required. Polyps and cancers should be measured using 2D images with lung window settings or 3D endoluminal views.
- Physician presence or immediate availability is required near CT scanning in the event of a colonic perforation or in the event of an allergic reaction to intravenous contrast.

Reading and Reporting

Reading

Intracolonic findings. All intracolonic findings should be examined, and any segment not adequately evaluated should be documented. All large masses and lesions that compromise luminal caliber should be communicated. The size and location of colorectal lesions should be reported, with appropriate images annotated or described. Descriptive features of polyps and masses should include morphologic features (sessile, pedunculated, flat), location (rectum, sigmoid, descending, transverse, ascending colon, cecum), and lesion attenuation (soft tissue attenuation and fat).

Extracolonic findings. Extracolonic findings (many of which are incidental findings) are common. In a recent systematic review involving 3488 patients, 40% of the patients had 1 or more abnormality. Extracolonic cancers were detected in 2.7% of patients, and 0.9% had an aortic aneurysm.[88] Approximately 1%–2% of patients will have highly important findings requiring medical or surgical intervention.[89,90] The incidence of extracolonic findings far surpasses the incidence of colorectal lesions of 5 mm in size,[88,91,92] but the large majority of these findings are not clinically significant and require no medical workup (eg, hiatal hernia, cholelithiasis, renal stone).

Typically, the detection and interpretation of extracolonic findings at CT colonography has been performed by radiologists, who have completed formal training programs and passed written and oral subspecialty examinations testing their ability to detect radiographic abnormalities. Radiologists are trained in the use of CT in a variety of practice settings not germane to the practice of CT colonography (eg, trauma, CT angiography, oncologic staging). Additionally, the occasional use of intravenous contrast will necessitate the identification of lesions unseen without intravenous contrast and the characterization of nonspecific abnormalities. These instances require extensive expertise in recognizing abnormalities of the lungs, solid organs, retroperitoneum, and the extracolonic gastrointestinal tract. Therefore, all extracolonic findings should be reported, and a radiologist should be consulted to properly examine the extracolonic portion of the study.

Task Force Recommendations

- CT colonography reading should include the size, morphologic features, and location of polyps and masses and lesion attenuation.
- Overall results and findings of the CT colonography examination should be adequately documented and communicated back to the referring physician and patient.
- Gastroenterologists should work collaboratively with board-certified radiologists to review the extracolonic portion of the CT colonography examination.
- All visualized extracolonic findings should be described, along with recommendations for further workup communicated back to the physician who ordered the test and the gastroenterologist who performed the CT colonography examination.

Reporting

Development of a standardized method of reporting CT colonography will be influenced by local practice, referral patterns, and methods of information dissemination (paper vs electronic). As such, the guidelines here are not intended to represent a standard but rather a framework for covering pertinent aspects of the patient encounter. Not surprisingly, the format of this report parallels that which has been proposed for colonoscopy[93] and incorporates elements developed by the American College of Radiology.[45,46]

Standardized report. The report should encompass elements of preprocedure documentation, patient demographics, indications, technical description, findings, clinical assessment, and recommendations (plan) for follow-up (Table 2). In particular, the preprocedure element should include patient education and a discussion of possible complications (eg, perforation) as well as the risk of missing significant lesions. Review of available alternatives to CT colonography for colonic evaluation is appropriate.

Polyp reporting. One of the most controversial areas in the field has to do with reporting of polyps. In

Table 2. Recommended Elements in CT Colonography Report

1. Preprocedure:
   - Preparation type and use of fecal tagging
   - Facility, equipment, and software used
   - IV contrast
   - Slice collimation (≤3 mm optimal, maximum is 5 mm) and reconstruction interval (≤1.5 mm is optimal, maximum is 2.5 mm)
   - Method of interpretation
     - Primary 2D
     - Primary 3D
2. Indication(s) for procedure:
   - Recommended documentation in all cases if known
     - Date of last examination and type (eg, colonoscopy, CT colonography)
     - Family history of colorectal cancer in first-degree relative
       - Number of family members
       - Age of index family member(s) who had colorectal cancer
       - Family history of adenoma in first-degree relative
     - Average risk
     - Family history of colorectal cancer (first-degree relative)
     - Family history of adenomatous polyps (first-degree relative)
     - Familial syndrome
       - FAP
       - HNPCC
3. Technical description:
   - Procedure date and time
   - Insufflation:
     - CO_2 or room air
     - Rectal balloon use
     - Technique (patient or technician controlled)
     - Use of antispasmodic (eg, glucagon)
     - Patient tolerance (good, fair, poor)
   - Position of patient for scanning:
     - Supine and prone
     - Additional views in decubitus
   - Quality of examination:
     - Preparation
     - Colon distention/visualization
       - Segments of colon not adequately distended
       - Segments of colon in which fluid/stool obscures visualization in all positions

4a. Findings: intracolonic
   - Colonic mass (lesion >3 cm)
     - Anatomic location (use standard terms of rectum, sigmoid colon, descending colon, transverse colon, ascending colon and cecum)
     - Maximum diameter with annotated images referenced in report
     - Morphology
       - Sessile: broad based with a width greater than vertical height
       - Pedunculated: polyp with separate stalk
       - Flat: polyp with vertical height less than 3 mm above surrounding normal colonic mucosa
     - Depth of invasion
     - Circumferential
     - Luminal narrowing (% compromised)
     - Regional lymphadenopathy
     - Distant metastases
   - Colonic polyp(s) (descriptors for each polyp)
     - Anatomic location
     - Maximum diameter (mm) with annotated images referenced in report
     - Morphology
       - Sessile: broad based with a width greater than vertical height
       - Pedunculated: polyp with separate stalk
       - Flat: polyp with vertical height less than 3 mm above surrounding normal colonic mucosa
   - Polyp cluster: multiple polyps (3 or more) in same anatomic region
     - Anatomic location
     - Size range: mm
     - Approximate number in a segment
     - Morphology (sessile/pedunculated/flat)
   - Fat attenuation lesion
     - Anatomic location
     - Size: mm

Table 2. (Continued)

Mucosal abnormality
Suspected diagnosis: ulcerative colitis, Crohn's disease, ischemia, infection, and others
Anatomic location/extent
Other findings:
Diverticulosis
Arteriovenous malformations
Hemorrhoids
Other
4b. Findings: extracolonic
E0: limited examination. Compromised by artifact; evaluation of extracolonic soft tissues is severely limited.
E1: normal examination or anatomic variant. No extracolonic abnormalities visible
Anatomic variant: eg, retroaortic left renal vein, replaced hepatic artery arising from the superior mesenteric artery
E2: clinically unimportant finding. No workup indicated.
Liver, kidney: simple cysts
Gallbladder: cholelithiasis without cholecystitis
Vetebra: hemangioma
E3: likely unimportant finding, incompletely characterized. Workup may be indicated depending on local practice and patient preference.
Kidney: minimally complex or homogeneously hyperattenuating cyst
Gallbladder: cholelithiasis without cholecystitis
Vetebra: hemangioma
E4: potentially important finding. Method of communication to referring physician as per accepted practice guidelines (eg, telephone call, written report).
Kidney: solid mass
Lymphadenopathy
Vasculature: aortic aneurysm
Lung: nonuniformly calcified parenchymal nodule ≥1 cm
5. Interventions/unplanned events
Events and unplanned interventions during or immediately after CT colonography
Type of event (eg, vasovagal, perforation)
Type of intervention
6. Assessment and follow-up plan
Should be based on history, symptoms, and CT colonography findings
Documentation of communication directly to the patient and referring MD

FAP, familial adenomatous polyposis; HNPCC, hereditary nonpolyposis colorectal cancer.

patients undergoing the examination for screening, polyp size remains one of the most important criterion by which a given lesion could be stratified with respect to the risk of developing into cancer.[94] The detection and reporting of colorectal polyps is affected by multiple considerations including the screening and surveillance recommendations, the natural history of subcentimeter polyps, the performance (sensitivity and specificity) of CT colonography for polyps of different sizes, the accuracy of polyp measurement at CT colonography, and the selection of CT colonography acquisition parameters and bowel tagging regimens.[12,29,93,95,96] Even CT colonography studies that have reported satisfactory results for polyps 6–9 mm in size report poor performance for polyps 5 mm or smaller in size.[9,73]

General agreement exists that all polyps ≥10 mm should be reported and the patient referred to endoscopic polypectomy because 10%–25% of these lesions will harbor high-grade dysplasia or cancer.[97] However, full consensus relating to the reporting or management of subcentimeter polyps discovered at CT colonography has not been reached among all groups.[12,93,98,99] It is generally agreed that the presence of 3 or more small polyps increases the risk of developing colorectal cancer.[96] In the recent CT colonography reporting and data system consensus proposal, for the purposes of screening, 6 mm was suggested as the minimum size for reporting polyp lesions.[93] This viewpoint was endorsed by the European Society of Gastrointestinal and Radiology in a recent consensus statement that recommends polyps 4 mm or smaller should be ignored, and a significant minority among the faculty would ignore 5-mm polyps, even when multiple.[100] The practice guidelines of the American College of Radiology for the performance of CT colonography in adults state that the reporting of polyps ≤5 mm is not recommended.[46] Current American College of Gastroenterology recommendations state that patients with polyps ≥6 mm and patients with 3 or more polyps of any size should be offered colonoscopy and polypectomy.[95] It also recommends that polyps of any size detected with moderate to high confidence should be reported because patients and referring physicians deserve to be aware of the test results.

The referral of patients to endoscopy for diminutive lesions (when CT colonography specificity is low) could lead to a large number of patients being referred to endoscopy[95] and compromise productivity at subsequent endoscopy. Moreover, current CT colonography acquisi-

tion parameters (principally slice thickness and radiation dose) are tailored to the detection of polyps 6 to 10 mm in diameter, but thinner slices or increased dose might improve performance.[71,72] Based on these considerations, it is recommended that all polyps 6 mm or larger should be reported but that smaller lesions need not be reported and should only be reported when reader confidence is very high.

Task Force Recommendations

- CT colonography findings should be communicated to the patient as well as the patient's referring physician in a timely manner through direct contact with the patient and a standardized report back to the physician (Table 2).
- Any polyp ≥6 mm should be reported and the patient referred for consideration of endoscopic polypectomy.
- Patients with 3 or more polyps of any size in the setting of high diagnostic confidence (The level of diagnostic confidence should be assessed by the examining physician based on patient history, the size of lesion[s], appearance of lesion[s], clinician experience with the procedure, the quality of preparation, the level of distention, and the overall quality of the examination.) should be referred for consideration of endoscopic polypectomy.
- Patients with 1 or 2 lesions each no greater than 5 mm may not need to be reported but can be reported when diagnostic confidence is high. Insufficient data exist to recommend a follow-up interval for repeat study for these patients and whether it should be radiologic CT, colonoscopy, or one of other evolving methods. In the absence of data, the follow-up interval recommended for these patients should be based on individual characteristics of the patient and procedure.
- Further investigation is recommended to understand better the natural history of colon polyps and to facilitate the most appropriate clinical path.

Quality Control and Safety

A comprehensive technical and professional quality control program is necessary. Technical quality control should encompass both the CT scanner and the CT colonography workstation. In addition to routine quality control, facilities performing CT colonography must ensure that all rooms containing x-ray devices are appropriately shielded for radiation in accordance with all federal and state regulations (NRC Regulations; http://www.nrc.gov/reading-rm/doc-dollections/cfr/part020/full-tex.html). Annual testing should include uniformity testing of CT number as well as spatial resolution, with visibility to 5-line pairs/cm bar pattern clearly resolved (http://www.acr.org/accreditation/computed/ct_qc_forms_html). Daily testing should include manufacturer or water phantom testing of CT number and noise, depending on state regulatory requirements. The CT colonography workstation monitor should undergo weekly Society of Motion Picture and Television Engineers (SMPTE) or equivalent video test pattern testing showing lack of aliasing of bar patterns and other artifacts with 95% and 5% squares visible.[101]

Professional quality assessment monitors outcomes relating to established metrics within a practice. It is anticipated that, over time, national benchmarks for CT colonography performance will be established, which can serve to improve quality and potentially guide reimbursement.[102,103] A National Radiology Data Registry is under development that could serve as an "overarching" registry in which modality specific data (eg, positron emission tomography scans and CT colonography) could be entered.[104] For internal quality assessment purposes, practices should establish mechanisms to track endoscopic findings in patients referred to colonoscopy so that true-positive rate, false-positive rate, and sensitivity in referred patients can be calculated. The number of "inadequate" examinations, in which full assessment of the colorectum is precluded by excess stool, fluid, or collapse should also be recorded. The adequacy of the preparation, the appropriateness of the follow-up recommendations, and the prompt notification of the patient and the referring physician should also be tracked. Any complications at CT colonography should be recorded, along with any predisposing conditions (such as obstructing lesions, concomitant colonic disease, or type of insufflation).[105] Such measures will alert physicians that changes may need to be made in patient educational materials, patient preparation regimens, or interpretation techniques.

Retrospective, sporadic review of CT colonography parameters and reports can also ensure that appropriate technique and practice patterns are being followed. In particular, retrospective review of technical parameters in average-sized patients should measure compliance with standard acquisition protocols, ensuring low-dose, high spatial resolution technique. Additionally, random CT colonography reports should be reviewed to ensure compliance with guidelines, ensuring that they include information summarizing technique, polyp location, and size and presence of significant extracolonic pathology.

Standardized practices followed by all physicians and allied health personnel within a practice can also improve patient safety. Practices should establish their own policies with respect to the use of intravenous iodinated contrast (eg, indications, rate and amount of administration, contraindications, treatment of adverse reactions).

Task Force Recommendations

- Practices should establish a technical quality control program that monitors spatial resolution, CT number, and noise of CT systems and grey scale of CT colonography computer workstation monitors.
- Professional quality control should include tracking of endoscopic results in patients referred to endoscopy from CT colonography so that true-positive and false-negative rates can be tracked.
- The frequency of "inadequate" examinations and complications should be recorded.
- Random sampling of CT colonography images and reports should be performed to measure compliance with low-dose, high spatial resolution techniques and standardized reporting guidelines.
- Practices should establish their own policies and procedures with respect to the use of iodinated intravenous contrast.

Regulatory Issues

Several regulatory issues affect the gastroenterologist's decision to perform CT colonography including the following: (1) who can perform the service; (2) split interpretation, in which one physician interprets intracolonic images and another performs the extracolonic images; and (3) risk management issues.

Who Can Perform CT Colonography: Implications of Stark Laws

The first consideration with regard to who is allowed to perform CT colonography centers around the concept of self-referral or "kickback." Concern that kickback schemes could corrupt the professional judgment of referring physicians and result in overutilization or ordering unnecessary items and services led to the 1972 Federal Anti-kickback Law.[106] Since its creation, the original anti-kickback statute has been revised to allow more than 20 exceptions or "safe harbors" such as for investments in group practices, small health care joint ventures, space rental, and equipment rental. In 1989, Congress passed "Stark I," prohibiting a physician from referring Medicare patients to an entity for clinical laboratory services if the physician (or their immediate family member) has a financial relationship with that entity. In 1993, "Stark II" expanded the Medicare self-referral ban to prohibit physicians from referring "designated health services" to an entity with which the physician has a financial relationship, unless that financial relationship meets an exception.[107,108] The definition of "designated health services" is key and includes, among other things, radiology and certain other imaging services, including ultrasound, CT, magnetic resonance imaging, and nuclear medicine. Both performing and interpreting CT colonography constitute designated health services.[109] Sanctions for violating the Stark statutes are severe, including refunds to the Medicare program, civil monetary penalties, and, under some circumstances, exclusion from the Medicare and Medicaid programs.

Referrals

The Stark statute defines referral very broadly to include the request by a physician for an item or service. Regulations clarify that a physician does not make a referral when he or she personally performs a service. However, a service is not personally performed if it is provided by any other person, including but not limited to the referring physician's employees, independent contractors, or group practice members. Stark prohibits referrals only if the physician has a financial relationship with the entity to which the referral is made. A financial relationship may consist of an ownership, investment interest, or a compensation arrangement that can be direct or indirect. An indirect financial relationship could arise, for example, if a physician has a contract with, or ownership in, an entity such as an imaging center that has a contract with a hospital to which the physician refers. An indirect ownership interest may pierce through several "holding companies" or layers of ownership established as an intermediary entity through which revenues obtained from referrals, for example, would be distributed to the physicians proportionally to their ownership interests and/or capital investment but not directly based on the volume of referrals.

The Stark regulations clarify that an indirect ownership interest will trigger Stark sanctions only if the entity furnishing the designated health services has actual knowledge of or acts in reckless disregard or deliberate ignorance of the fact that the referring physician (or an immediate family member) has some ownership or investment interest in the entity.[110]

Split Interpretation and Billing for Services

Billing for CT colonography services when a gastroenterologist furnishes the interpretation of the colonic images and a radiologist furnishes the interpretation of the extracolonic findings appears to be a complicated issue but could be accomplished in several ways. If a gastroenterologist refers the CT colonography to a radiology group or imaging center that bills for the service, and the gastroenterologist is compensated by the group/center for interpreting the colonic images, the gastroenterologist's compensation would need to meet the Stark Personal Services or Fair Market Value exceptions. If the gastroenterologist is engaged by the group/center through the gastroenterologist's group practice, the compensation would need to satisfy an indirect compensation arrangement analysis.[111] Unfortunately, there is no clear definition of "fair market value." Physicians should not base rates on internally generated analyses,

and fair market values cannot be based on the volume or value of referrals to the physician. Each of the exceptions has additional technical requirements that would need to be satisfied and should be researched further prior to entering into a relationship.

If the gastroenterologist bills for the entire interpretation, but enters into an arrangement with a radiologist to perform a portion, the threshold Stark question is whether the radiologist is furnishing a designated health service. The conservative approach would be for the radiologist to be employed on a part-time basis by the gastroenterology group, or for the gastroenterologist to perform the entire interpretation with a radiologist "overread," so as to strengthen the argument that the radiologist has not in fact furnished a designated health service billed for by the group.

Currently, 2 category III current procedural terminology (CPT) codes (0066T, 0067T) could be used for CT colonography: 1 for screening studies and 1 for diagnostic. Category III codes are temporary codes used to track emerging technologies, services, and procedures.[112] Medicare does not set specific reimbursement criteria for these codes; therefore, payment for a category III code is up to the discretion of the specific carriers.[113] The 2 existing codes capture the work associated with the interpretation of all images gathered from the study. No current CPT modifiers could be appropriately used to reflect a split interpretation by 2 different specialists. Therefore, it appears that the service must be billed by one of the 2 interpreting physicians, with the billing physician separately reimbursing the nonbilling physician for his or her interpretation service.

Split interpretation arrangements are potentially problematic because the Centers for Medicare & Medicade Services-1500 claim form requires certification by the billing physician that "the services shown on this form . . . were personally furnished by (the billing physician) or were furnished incident to (his or her) professional service by (his or her) employee under . . . immediate personal supervision." In situations in which the billing physician interprets only a portion of the CT study, he or she may be falsely certifying that he or she furnished all services; this could be construed as a false claim.

A conservative approach to coding and reimbursement-related concerns would be for the gastroenterologist to perform an interpretation of all images and contract with the radiologist for an overread. The gastroenterologist could argue that he or she has "personally furnished" all of the services claimed. In a presumed split interpretation arrangement, the patient would be referred for the CT colonography by the gastroenterologist, who will bill for the interpretation and contract with the radiologist, on a fixed per-interpretation basis, to perform or overread the extracolonic image interpretation. This arrangement, however, potentially implicates the Federal Anti-kickback Law because it could be alleged that the radiologist is providing remuneration in the form of discounted services in exchange for this referral or other unrelated referrals. Accurately defining "fair market value," therefore, is critical. Unfortunately, no statute or regulation defines "fair market value" under the Federal Anti-kickback Law. The gastroenterologist can minimize exposure under the kickback law by not setting lower fees for the split interpretation in return for the referral or the promise of other business that the radiologist could bill directly.

The only potentially applicable "safe harbor" for a compensation arrangement between the gastroenterologist and the radiologist in a split interpretation or overread arrangement is the personal services and management agreements safe harbor,[114] an agreement in advance between 2 physicians that specifies the schedule and precise length of work to be furnished and the aggregate compensation paid over the term of the agreement. In developing such an agreement, the gastroenterologist and radiologist should consult with legal counsel and ensure that the agreement includes at least (1) a specific time frame, (2) the specifics of reimbursement, (3) the parameters of each physician's responsibility, (4) the basis for splitting the interpretation, (5) which physician is responsible for recommending additional diagnostic tests or consults with other specialists, and (6) which physician is responsible for communicating the interpretation results to the patient and for managing the patient's course of treatment.

Oversight

For diagnostic tests payable under the Medicare Physician Fee Schedule, CT studies without contrast require "general supervision." This stipulates that, although the physician's presence is not required during the performance of the procedure, the training of the nonphysician technician who actually performs the test and the maintenance of the necessary equipment and supplies are the continuing responsibility of the supervising physician. CT studies with contrast require "direct supervision," meaning the physician must be present in the office suite and immediately available to furnish assistance and direction throughout the procedure.[115]

Risk Management Issues

Split interpretations also raise a risk management issue as to whether the gastroenterologist is clinically competent to read colonic and extracolonic images without assistance from a radiologist and, furthermore, whether the radiologist or the gastroenterologist could be held liable for the errors or omissions of the other in connection with their respective interpretations of the CT colonography source images.

The premise that a split interpretation is medically necessary, and indeed clinically preferable, is based on the twin assumptions that (1), although the radiologist is

presumptively qualified (as a matter of education and experience but also by community standard) to provide an interpretation of all source images, the gastroenterologist is qualified to interpret the colonic images and is arguably the more appropriate professional to conduct that portion of the review based on a combination of that physician's training and clinical knowledge of the particular patient; and (2), although the gastroenterologist may be competent to interpret the colonic images, the gastroenterologist may not be best qualified to interpret the extracolonic images absent specialized training and experience akin to that of a radiologist.

The second major risk management question posed by a split interpretation arrangement is whether the gastroenterologist could be held liable for an incorrect or incomplete interpretation of the radiologist. A further question is whether the physician who signs the report is affirming the other physician's interpretation and is therefore assuming any liability associated with that interpretation.

State laws governing medical malpractice determine whether and how physicians can be held liable for the errors and omissions of another physician and how any such liability will be apportioned. Regardless, a malpractice action alleging negligence based directly or indirectly on an interpretation of a set of images will typically include as defendants all physicians who played any role in interpreting those images. As such, there is little that can be done to reduce the risk of a gastroenterologist being named in a lawsuit that involves a split interpretation. To reduce the risk that the gastroenterologist will ultimately be held liable for the acts or omissions of the radiologist, it is recommended that each physician should sign a separate report: the gastroenterologist of his/her interpretation of the colonic images and the radiologist a report of his/her interpretation of the extracolonic images. The report form could include a statement indicating that the radiologist's interpretation is included therein but is not independently validated by the gastroenterologist. Although this might limit the gastroenterologist's potential liability for the professional negligence of the radiologist, this approach would increase the potential false certification and Stark risks as compared with an approach by which the gastroenterologist issues a single report that incorporates the radiologist's overread findings.

The education provided to the patient should expressly include the fact that both the gastroenterologist and the radiologist will be interpreting the images and the reasons therefore. The education should also identify for the patient which physician will discuss the results of the test with the patient and which physician will be in charge of any treatment decisions based on the interpretations.

A gastroenterologist who agrees to a split interpretation arrangement should prospectively consult with his or her malpractice carrier to obtain guidance from the carrier concerning limitations of coverage relating to such services and whether such limitations could be different in a split interpretation vs an overread arrangement.

Task Force Recommendations

- Split interpretations of CT colonography are feasible under federal anti-kickback and Stark laws.
- Physicians entering into a split interpretation agreement should seek counsel to develop a written split interpretation agreement.
- Gastroenterologists and radiologists performing split interpretations should dictate and sign separate procedure reports that clearly state the specific services they performed related to CT colonography.
- Gastroenterologists considering offering CT colonography should consult with their health care counsel regarding compliance with state and local regulations.

References

1. American Gastroenterological Association (AGA) Institute Position on computed tomographic colonography. Gastroenterology 2006;131:1627–1628.
2. Bar-Meir S, Wallace MB. Diagnostic colonoscopy: the end is coming. Gastroenterology 2006;131:992–994.
3. Rockey DC, Paulson E, Niedzwiecki D, Davis W, Bosworth HB, Sanders L, Yee J, Henderson J, Hatten P, Burdick S, Sanyal A, Rubin DT, Sterling M, Akerkar G, Bhutani MS, Binmoeller K, Garvie J, Bini EJ, McQuaid K, Foster WL, Thompson WM, Dachman A, Halvorsen R. Analysis of air contrast barium enema, computed tomographic colonography, and colonoscopy: prospective comparison. Lancet 2005;365:305–311.
4. Cotton PB, Durkalski VL, Pineau BC, Palesch YY, Mauldin PD, Hoffman B, Vining DJ, Small WC, Affronti J, Rex D, Kopecky KK, Ackerman S, Burdick JS, Brewington C, Turner MA, Zfass A, Wright AR, Iyer RB, Lynch P, Sivak MV, Butler H. Computed tomographic colonography (virtual colonoscopy): a multicenter comparison with standard colonoscopy for detection of colorectal neoplasia. JAMA 2004;291:1713–1719.
5. Pickhardt PJ, Choi JR, Hwang I, Butler JA, Puckett ML, Hildebrandt HA, Wong RK, Nugent PA, Mysliwiec PA, Schindler WR. Computed tomographic virtual colonoscopy to screen for colorectal neoplasia in asymptomatic adults. N Engl J Med 2003; 349:2191–2200.
6. Johnson CD, Harmsen WS, Wilson LA, Maccarty RL, Welch TJ, Ilstrup DM, Ahlquist DA. Prospective blinded evaluation of computed tomographic colonography for screen detection of colorectal polyps. Gastroenterology 2003;125:311–319.
7. Pineau BC, Paskett ED, Chen GJ, Espeland MA, Phillips K, Han JP, Mikulaninec C, Vining DJ. Virtual colonoscopy using oral contrast compared with colonoscopy for the detection of patients with colorectal polyps. Gastroenterology 2003;125: 304–310.
8. McFarland EG, Pilgram TK, Brink JA, McDermott RA, Santillan CV, Brady PW, Heiken JP, Balfe DM, Weinstock LB, Thyssen EP, Littenberg B. CT colonography: multiobserver diagnostic performance. Radiology 2002;225:380–390.
9. Yee J, Akerkar GA, Hung RK, Steinauer-Gebauer AM, Wall SD, McQuaid KR. Colorectal neoplasia: performance characteristics

of CT colonography for detection in 300 patients. Radiology 2001;219:685–692.
10. Fletcher JG, Johnson CD, Welch TJ, MacCarty RL, Ahlquist DA, Reed JE, Harmsen WS, Wilson LA. Optimization of CT colonography technique: prospective trial in 180 patients. Radiology 2000;216:704–711.
11. Fenlon HM, Nunes DP, Schroy PC, Barish MA, Clarke PD, Ferrucci JT. A comparison of virtual and conventional colonoscopy for the detection of colorectal polyps. N Engl J Med 1999;341: 1496–1503.
12. Van Dam J, Cotton P, Johnson CD, McFarland BG, Pineau BC, Provenzale D, Ransohoff D, Rex D, Rockey D, Wootton FT. AGA future trends report: CT colonography. Gastroenterology 2004; 127:970–984.
13. Rex DK, Cutler CS, Lemmel GT, Rahmani EY, Clark DW, Helper DJ, Lehman GA, Mark DG. Colonoscopic miss rates of adenomas determined by back-to-back colonoscopies. Gastroenterology 1997;112:24–28.
14. Hoppe H, Quattropani C, Spreng A, Mattich J, Netzer P, Dinkel HP. Virtual colon dissection with CT colonography compared with axial interpretation and conventional colonoscopy: preliminary results. AJR Am J Roentgenol 2004;182:1151–1158.
15. Rockey DC. Advances in Digestive Disease. In: Howden CW, ed. AGA Institute Press. Bethesda, MD, 2007:169–176.
16. Yoshida H, Nappi J, MacEneaney P, Rubin DT, Dachman AH. Computer-aided diagnosis scheme for detection of polyps at CT colonography. Radiographics 2002;22:963–979.
17. Yoshida H, Masutani Y, MacEneaney P, Rubin DT, Dachman AH. Computerized detection of colonic polyps at CT colonography on the basis of volumetric features: pilot study. Radiology 2002; 222:327–336.
18. Halligan S, Altman DG, Mallett S, Taylor SA, Burling D, Roddie M, Honeyfield L, McQuillan J, Amin H, Dehmeshki J. CT colonography: assessment of radiologist performance with and without computer-aided detection. Gastroenterology 2006;131:2006–2009.
19. Callstrom MR, Johnson CD, Fletcher JG, Reed JE, Ahlquist DA, Harmsen WS, Tait K, Wilson LA, Corcoran KE. CT colonography without cathartic preparation: feasibility study. Radiology 2001; 219:693–698.
20. Zalis ME, Perumpillichira J, Del Frate C, Hahn PF. CT colonography: digital subtraction bowel cleansing with mucosal reconstruction initial observations. Radiology 2003;226:911–917.
21. McFarland EG, Zalis ME. CT colonography: progress toward colorectal evaluation without catharsis. Gastroenterology 2004; 127:1623–1626.
22. Iannaccone R, Laghi A, Catalano C, Mangiapane F, Lamazza A, Schillaci A, Sinibaldi G, Murakami T, Sammartino P, Hori M, Piacentini F, Nofroni I, Stipa V, Passariello R. Computed tomographic colonography without cathartic preparation for the detection of colorectal polyps. Gastroenterology 2004;127:1300–1311.
23. Lefere P, Gryspeerdt S, Marrannes J, Baekelandt M, Van Holsbeeck B. CT colonography after fecal tagging with a reduced cathartic cleansing and a reduced volume of barium. AJR Am J Roentgenol 2005;184:1836–1842.
24. Zalis ME, Perumpillichira JJ, Magee C, Kohlberg G, Hahn PF. Tagging-based, electronically cleansed CT colonography: evaluation of patient comfort and image readability. Radiology 2006; 239:149–159.
25. Rex D, Imperiale T, Latinovich D, Bratcher LL. Impact of bowel preparation on efficiency and cost of colonoscopy. Am J Gastroenterol 2002;97:1696–1700.
26. Macari M, Berman P, Dicker M, Milano A, Megibow AJ. Usefulness of CT colonography in patients with incomplete colonoscopy. AJR Am J Roentgenol 1999;173:561–564.
27. Morrin MM, Kruskal JB, Farrell RJ, Goldberg SN, McGee JB, Raptopoulos V. Endoluminal CT colonography after an incomplete endoscopic colonoscopy. AJR Am J Roentgenol 1999;172: 913–918.
28. Fajobi O, Yiu CY, Sen-Gupta SB, Boulos PB. Metachronous colorectal cancers. Br J Surg 1998;85:897–901.
29. Smith RA, Cokkinides V, Eyre HJ. American Cancer Society guidelines for the early detection of cancer, 2006. CA Cancer J Clin 2006;56:11–25; quiz 49–50.
30. Fenlon HM, McAneny DB, Nunes DP, Clarke PD, Ferrucci JT. Occlusive colon carcinoma: virtual colonoscopy in the preoperative evaluation of the proximal colon. Radiology 1999;210: 423–428.
31. Galia M, Midiri M, Carcione A, Cusma S, Bartolotta TV, Angileri T, De Maria M, Lagalla R. Usefulness of CT colonography in the preoperative evaluation of patients with distal occlusive colorectal carcinoma. Radiol Med (Torino) 2001;101:235–242.
32. Gollub MJ, Ginsberg MS, Cooper C, Thaler HT. Quality of virtual colonoscopy in patients who have undergone radiation therapy or surgery: how successful are we? AJR Am J Roentgenol 2002; 178:1109–1116.
33. Lin OS, Kozarek RA, Schembre DB, Ayub K, Gluck M, Drennan F, Soon MS, Rabeneck L. Screening colonoscopy in very elderly patients: prevalence of neoplasia and estimated impact on life expectancy. JAMA 2006;295:2357–2365.
34. Hara AK, Johnson CD, Reed JE, Ahlquist DA, Nelson H, MacCarty RL, Harmsen WS, Ilstrup DM. Detection of colorectal polyps with CT colography: initial assessment of sensitivity and specificity. Radiology 1997;205:59–65.
35. Royster AP, Fenlon HM, Clarke PD, Nunes DP, Ferrucci JT. CT colonoscopy of colorectal neoplasms: two-dimensional and three-dimensional virtual-reality techniques with colonoscopic correlation. AJR Am J Roentgenol 1997;169:1237–1242.
36. Dachman AH, Kuniyoshi JK, Boyle CM, Samara Y, Hoffmann KR, Rubin DT, Hanan I. CT colonography with three-dimensional problem solving for detection of colonic polyps. AJR Am J Roentgenol 1998;171:989–995.
37. Rex DK, Vining D, Kopecky KK. An initial experience with screening for colon polyps using spiral CT with and without CT colography (virtual colonoscopy). Gastrointest Endosc 1999;50: 309–313.
38. Macari M, Bini EJ, Jacobs SL, Naik S, Lui YW, Milano A, Rajapaksa R, Megibow AJ, Babb J. Colorectal polyps and cancers in asymptomatic average-risk patients: evaluation with CT colonography. Radiology 2004;230:629–636.
39. Cash BD, Kim CH, Cullen PA, Kim M, Dykes CA, Jensen DW, Barlow DS, Johnston MH, Kikendall JW, Soballe PW. Accuracy of computed tomographic colonography for colorectal cancer (CRC) screening in asymptomatic, average risk individuals. Gastroenterology 2006;130:A46.
40. Mulhall BP, Veerappan GR, Jackson JL. Meta-analysis: computed tomographic colonography. Ann Intern Med 2005;142: 635–650.
41. Pignone M, Rich M, Teutsch SM, Berg AO, Lohr KN. Screening for colorectal cancer in adults at average risk: a summary of the evidence for the US Preventive Services Task Force. Ann Intern Med 2002;137:132–141.
42. Winawer S, Fletcher R, Rex D, Bond J, Burt R, Ferrucci J, Ganiats T, Levin T, Woolf S, Johnson D, Kirk L, Litin S, Simmang C. Colorectal cancer screening and surveillance: clinical guidelines and rationale—update based on new evidence. Gastroenterology 2003;124:544–560.
43. Pickhardt PJ, Taylor AJ, Kim DH, Reichelderfer M, Gopal DV, Pfau PR. Screening for colorectal neoplasia with CT colonography: initial experience from the first year of coverage by third-party payers. Radiology 2006;241:417–425.

44. Gluecker TM, Fletcher JG, Welch TJ, MacCarty RL, Harmsen WS, Harrington JR, Ilstrup D, Wilson LA, Corcoran KE, Johnson CD. Characterization of lesions missed on interpretation of CT colonography using a 2D search method. AJR Am J Roentgenol 2004;182:881–889.
45. ACR practice guideline for performing and interpreting diagnostic computed tomography (CT). ACR Practice Guideline 2002 (Res. 2) 2002:27–30.
46. ACR practice guideline for the performance of computed tomography (CT) colonography in adults. ACR Practice Guideline 2002 (Res. 2) 2005;29:295–299.
47. Gastroenterology Core Curriculum, Third edition. Gastroenterology 2007;132:2012–2018.
48. Gluecker T, Meuwly JY, Pescatore P, Schnyder P, Delarive J, Jornod P, Meuli R, Dorta G. Effect of investigator experience in CT colonography. Eur Radiol 2002;12:1405–1409.
49. Spinzi G, Belloni G, Martegani A, Sangiovanni A, Del Favero C, Minoli G. Computed tomographic colonography and conventional colonoscopy for colon diseases: a prospective, blinded study. Am J Gastroenterol 2001;96:394–400.
50. Bodily KD, Fletcher JG, Engelby T, Percival M, Christensen JA, Young B, Krych AJ, Vander Kooi DC, Rodysill D, Fidler JL, Johnson CD. Nonradiologists as second readers for intraluminal findings at CT colonography. Acad Radiol 2005;12:67–73.
51. Taylor SA, Halligan S, Burling D, Morley S, Bassett P, Atkin W, Bartram CI. CT colonography: effect of experience and training on reader performance. Eur Radiol 2004;14:1025–1033.
52. Slater A, Taylor SA, Tam E, Gartner L, Scarth J, Peiris C, Gupta A, Marshall M, Burling D, Halligan S. Reader error during CT colonography: causes and implications for training. Eur Radiol 2006;16:2275–2283.
53. Budoff MJ, Cohen MC, Garcia MJ, Hodgson JM, Hundley WG, Lima JA, Manning WJ, Pohost GM, Raggi PM, Rodgers GP, Rumberger JA, Taylor AJ, Creager MA, Hirshfeld JW Jr, Lorell BH, Merli G, Rodgers GP, Tracy CM, Weitz HH. ACCF/AHA clinical competence statement on cardiac imaging with computed tomography and magnetic resonance: a report of the American College of Cardiology Foundation/American Heart Association/American College of Physicians Task Force on Clinical Competence and Training. J Am Coll Cardiol 2005;46:383–402.
54. Baker M, Obuchowsky N, Dass C, Kendzierski R, Einstein D, Remer E. Efficacy of computer-aided detection of colorectal polyps when applied to initial, inexperienced radiologist interpretations of CT colonography: a pilot study. RSNA 2005:337A.
55. Summers RM, Yao J, Pickhardt PJ, Franaszek M, Bitter I, Brickman D, Krishna V, Choi JR. Computed tomographic virtual colonoscopy computer-aided polyp detection in a screening population. Gastroenterology 2005;129:1832–1844.
56. Wexner SD, Beck DE, Baron TH, Fanelli RD, Hyman N, Shen B, Wasco KE. A consensus document on bowel preparation before colonoscopy: prepared by a task force from the American Society of Colon and Rectal Surgeons (ASCRS), the American Society for Gastrointestinal Endoscopy (ASGE), and the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES). Gastrointest Endosc 2006;63:894–909.
57. Lefere PA, Gryspeerdt SS, Dewyspelaere J, Baekelandt M, Van Holsbeeck BG. Dietary fecal tagging as a cleansing method before CT colonography: initial results polyp detection and patient acceptance. Radiology 2002;224:393–403.
58. Macari M, Lavelle M, Pedrosa I, Milano A, Dicker M, Megibow AJ, Xue X. Effect of different bowel preparations on residual fluid at CT colonography. Radiology 2001;218:274–277.
59. Bosworth HB, Rockey DC, Paulson EK, Niedzwiecki D, Davis W, Sanders LL, Yee J, Henderson J, Hatten P, Burdick S, Sanyal A, Rubin DT, Sterling M, Akerkar G, Bhutani MS, Binmoeller K, Garvie J, Bini EJ, McQuaid K, Foster WL, Thompson WM, Dachman A, Halvorsen R. Prospective comparison of patient experience with colon imaging tests. Am J Med 2006;119:791–799.
60. Pickhardt PJ, Choi JH. Electronic cleansing and stool tagging in CT colonography: advantages and pitfalls with primary three-dimensional evaluation. AJR Am J Roentgenol 2003;181:799–805.
61. Fenlon HM, Royster AP, Clarke PD, Ferrucci JT. Virtual colonoscopy in the pre-operative evaluation of patients with obstructing colorectal carcinoma. Radiology 1997;205:195A.
62. Shinners TJ, Pickhardt PJ, Taylor AJ, Jones DA, Olsen CH. Patient-controlled room air insufflation versus automated carbon dioxide delivery for CT colonography. AJR Am J Roentgenol 2006;186:1491–1496.
63. Yee J, Hung RK, Akerkar GA, Wall SD. The usefulness of glucagon hydrochloride for colonic distention in CT colonography. AJR Am J Roentgenol 1999;173:169–172.
64. Burling D, Taylor SA, Halligan S, Gartner L, Paliwalla M, Peiris C, Singh L, Bassett P, Bartram C. Automated insufflation of carbon dioxide for MDCT colonography: distention and patient experience compared with manual insufflation. AJR Am J Roentgenol 2006;186:96–103.
65. Young BM, Fletcher JG, Earnest F, Fidler JL, MacCarty RL, Johnson CD, Huprich JE, Hough D. Colonic perforation at CT colonography in a patient without known colonic disease. AJR Am J Roentgenol 2006;186:119–121.
66. Chen SC, Lu DS, Hecht JR, Kadell BM. CT colonography: value of scanning in both the supine and prone positions. AJR Am J Roentgenol 1999;172:595–599.
67. Hara AK, Johnson CD, MacCarty RL, Welch TJ, McCollough CH, Harmsen WS. CT colonography: single- versus multi-detector row imaging. Radiology 2001;219:461–465.
68. Kalra MK, Naz N, Rizzo SM, Blake MA. Computed tomography radiation dose optimization: scanning protocols and clinical applications of automatic exposure control. Curr Probl Diagn Radiol 2005;34:171–181.
69. Kalra MK, Rizzo SM, Novelline RA. Reducing radiation dose in emergency computed tomography with automatic exposure control techniques. Emerg Radiol 2005;11:267–274.
70. Laghi A, Lannaccone R, Panebianco V, Carbone L, Passariello R. Multislice CT colonography: technical developments. Semin Ultrasound CT MR 2001;22:425–431.
71. Taylor SA, Halligan S, Bartram CI, Morgan PR, Talbot IC, Fry N, Saunders BP, Khosraviani K, Atkin W. Multi-detector row CT colonography: effect of collimation, pitch, and orientation on polyp detection in a human colectomy specimen. Radiology 2003;229:109–118.
72. Wessling J, Fischbach R, Meier N, Allkemper T, Klusmeier J, Ludwig K, Heindel W. CT colonography: protocol optimization with multi-detector row CT—study in an anthropomorphic colon phantom. Radiology 2003;228:753–759.
73. Laghi A, Iannaccone R, Carbone I, Catalano C, Di Giulio E, Schillaci A, Passariello R. Detection of colorectal lesions with virtual computed tomographic colonography. Am J Surg 2002;183:124–131.
74. Macari M, Bini EJ, Xue X, Milano A, Katz SS, Resnick D, Chandarana H, Krinsky G, Klingenbeck K, Marshall CH, Megibow AJ. Colorectal neoplasms: prospective comparison of thin-section low-dose multi-detector row CT colonography and conventional colonoscopy for detection. Radiology 2002;224:383–392.
75. van Gelder RE, Venema HW, Serlie IW, Nio CY, Determann RM, Tipker CA, Vos FM, Glas AS, Bartelsman JF, Bossuyt PM, Lameris JS, Stoker J. CT colonography at different radiation dose levels: feasibility of dose reduction. Radiology 2002;224:25–33.
76. Iannaccone R, Laghi A, Catalano C, Brink JA, Mangiapane F, Trenna S, Piacentini F, Passariello R. Detection of colorectal lesions: lower-dose multi-detector row helical CT colonography

compared with conventional colonoscopy. Radiology 2003;229:775–781.
77. Johnson CD, Toledano AY, Herman BA, Dachman AH, McFarland EG, Barish MA, Brink JA, Ernst RD, Fletcher JG, Halvorsen RA, Jr., Hara AK, Hopper KD, Koehler RE, Lu DS, Macari M, Maccarty RL, Miller FH, Morrin M, Paulson EK, Yee J, Zalis M. Computerized tomographic colonography: performance evaluation in a retrospective multicenter setting. Gastroenterology 2003;125: 688–695.
78. Kemerink GJ, Borstlap AC, Frantzen MJ, Schultz FW, Zoetelief J, van Engelshoven JM. Patient and occupational dosimetry in double contrast barium enema examinations. Br J Radiol 2001; 74:420–428.
79. Brenner DJ, Georgsson MA. Mass screening with CT colonography: should the radiation exposure be of concern? Gastroenterology 2005;129:328–337.
80. Morrin MM, Farrell RJ, Kruskal JB, Reynolds K, McGee JB, Raptopoulos V. Utility of intravenously administered contrast material at CT colonography. Radiology 2000;217:765–771.
81. Macari M, Milano A, Lavelle M, Berman P, Megibow AJ. Comparison of time-efficient CT colonography with two- and three-dimensional colonic evaluation for detecting colorectal polyps. AJR Am J Roentgenol 2000;174:1543–1549.
82. Barish MA, Soto JA, Ferrucci JT. Consensus on current clinical practice of virtual colonoscopy. AJR Am J Roentgenol 2005;184: 786–792.
83. Pickhardt PJ. Three-dimensional endoluminal CT colonography (virtual colonoscopy): comparison of three commercially available systems. AJR Am J Roentgenol 2003;181:1599–1606.
84. McFarland EG, Brink JA, Pilgram TK, Heiken JP, Balfe DM, Hirselj DA, Weinstock L, Littenberg B. Spiral CT colonography: reader agreement and diagnostic performance with two- and three-dimensional image-display techniques. Radiology 2001;218: 375–383.
85. Fidler JL, Johnson CD, MacCarty RL, Welch TJ, Hara AK, Harmsen WS. Detection of flat lesions in the colon with CT colonography. Abdom Imaging 2002;27:292–300.
86. Pickhardt PJ, Lee AD, McFarland EG, Taylor AJ. Linear polyp measurement at CT colonography: in vitro and in vivo comparison of two-dimensional and three-dimensional displays. Radiology 2005;236:872–878.
87. Young BM, Fletcher JG, Paulsen SR, Booya F, Johnson CD, Johnson KT, Melton Z, Rodysill D, Mandrekar J. Polyp measurement with CT colonography: multiple-reader, multiple-workstation comparison. AJR Am J Roentgenol 2007;188: 122–129.
88. Xiong T, Richardson M, Woodroffe R, Halligan S, Morton D, Lilford RJ. Incidental lesions found on CT colonography: their nature and frequency. Br J Radiol 2005;78:22–29.
89. Hara AK, Johnson CD, MacCarty RL, Welch TJ. Incidental extracolonic findings at CT colonography. Radiology 2000;215:353–357.
90. Gluecker TM, Johnson CD, Wilson LA, Maccarty RL, Welch TJ, Vanness DJ, Ahlquist DA. Extracolonic findings at CT colonography: evaluation of prevalence and cost in a screening population. Gastroenterology 2003;124:911–916.
91. Miao YM, Amin Z, Healy J, Burn P, Murugan N, Westaby D, Allen-Mersh TG. A prospective single centre study comparing computed tomography pneumocolon against colonoscopy in the detection of colorectal neoplasms. Gut 2000;47:832–837.
92. Robinson P, Burnett H, Nicholson DA. The use of minimal preparation computed tomography for the primary investigation of colon cancer in frail or elderly patients. Clin Radiol 2002;57: 389–392.
93. Zalis ME, Barish MA, Choi JR, Dachman AH, Fenlon HM, Ferrucci JT, Glick SN, Laghi A, Macari M, McFarland EG, Morrin MM, Pickhardt PJ, Soto J, Yee J. CT colonography reporting and data system: a consensus proposal. Radiology 2005;236:3–9.
94. Bond JH. Screening guidelines for colorectal cancer. Am J Med 1999;106:S7–S10.
95. Rex DK, Lieberman D. ACG colorectal cancer prevention action plan: update on CT-colonography. Am J Gastroenterol 2006; 101:1410–1413.
96. Winawer SJ, Zauber AG, Fletcher RH, Stillman JS, O'Brien MJ, Levin B, Smith RA, Lieberman DA, Burt RW, Levin TR, Bond JH, Brooks D, Byers T, Hyman N, Kirk L, Thorson A, Simmang C, Johnson D, Rex DK. Guidelines for colonoscopy surveillance after polypectomy: a consensus update by the US Multi-Society Task Force on Colorectal Cancer and the American Cancer Society. Gastroenterology 2006;130:1872–1885.
97. Rex DK, Johnson DA, Lieberman DA, Burt RW, Sonnenberg A. Colorectal cancer prevention 2000: screening recommendations of the American College of Gastroenterology. American College of Gastroenterology. Am J Gastroenterol 2000;95:868–877.
98. Rex DK. PRO: Patients with polyps smaller than 1 cm on computed tomographic colonography should be offered colonoscopy and polypectomy. Am J Gastroenterol 2005;100:1903–1905; discussion 1907–1908.
99. Ransohoff DF. CON: Immediate colonoscopy is not necessary in patients who have polyps smaller than 1 cm on computed tomographic colonography. Am J Gastroenterol 2005;100: 1905–1907; discussion 1907–1908.
100. Taylor SA, Laghi A, Lefere P, Halligan S, Stoker J. European society of gastrointestinal and abdominal radiology (ESGAR): consensus statement on CT colonography. Eur Radiol 2007;17: 575–579.
101. 147 NRN. Structural shielding design for medical x-ray imaging. National Council for Radiation Protection & Measurements B, Maryland. 2004:20814–30945.
102. Johnson C, Swensen S, Applegate K, Blackmore C, Borgstede J, Cardella J, Dilling J, Dunnick N, Glenn L, Hillman B, Lau L, Lexa F, Weinreb J, Wilcox P. Quality improvement in radiology: white paper report of the Sun Valley Group Meeting. J Am Coll Radiol 2006;3:544–549.
103. Swensen SJ, Johnson CD. Radiologic quality and safety: mapping value into radiology. J Am Coll Radiol 2005;2:992–1000.
104. Moser JW, Wilcox PA, Bjork SS, Cushing T, Dennis M, Greissing JE, Keysor K, McKenzie J, et al. Pay for performance in radiology: ACR white paper. J Am Coll Radiol 2006;3:650–664.
105. Limburg PJ, Fletcher JG. Making sense of CT colonography-related complication rates. Gastroenterology 2006;131:2023–2024.
106. 42 USC §1320a-7b(b). Available at: http://www.aaasc.org/advocacy/documents/WDC99_937585_1.PDF. Accessed March 12, 2007.
107. Centers for Medicare and Medicaid Services, Physician Self-Referral Section. Available at: http://www.cms.hhs.gov/PhysicianSelfReferral/01_overview.asp#TopOfPage. Accessed March 12, 2007.
108. 42 USC §1320a-7b(b), United States Code: Title 42, 1320a-7b. Criminal penalties for acts involving Federal health care programs and 42 USC §1395nn, United States Code: Title 42, 1395nn. Limitation on certain physician referrals. Available at: http://www.cms.hhs.gov/PhysicianSelfReferral/Downloads/section_1877.pdf. Accessed March 12, 2007.
109. 42 CFR §411.351.
110. 42 CFR §411.354.
111. 42 CFR §411.357(d) and (l).
112. http://www.ama-assn.org/ama1/pub/upload/mm/362/07catiiicodes4507.pdf. American Medical Association, Category III Codes. Accessed June 29, 2007.

113. 66 Federal Register 55269 (November 1, 2001).
114. 42 CFR §1001.952(d).
115. Medicare Part B Reference Manual: Appendix L - Physician Supervision of Diagnostic Tests. http://www.highmarkmedicareservices.com/partb/refman/appendix-l.html. Accessed June 29, 2007.

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ACR PRACTICE GUIDELINE FOR THE PERFORMANCE OF COMPUTED TOMOGRAPHY (CT) COLONOGRAPHY IN ADULTS

PREAMBLE

These guidelines are an educational tool designed to assist practitioners in providing appropriate radiologic care for patients. They are not inflexible rules or requirements of practice and are not intended, nor should they be used, to establish a legal standard of care. For these reasons and those set forth below, the American College of Radiology cautions against the use of these guidelines in litigation in which the clinical decisions of a practitioner are called into question.

The ultimate judgment regarding the propriety of any specific procedure or course of action must be made by the physician or medical physicist in light of all the circumstances presented. Thus, an approach that differs from the guidelines, standing alone, does not necessarily imply that the approach was below the standard of care. To the contrary, a conscientious practitioner may responsibly adopt a course of action different from that set forth in the guidelines when, in the reasonable judgment of the practitioner, such course of action is indicated by the condition of the patient, limitations on available resources, or advances in knowledge or technology subsequent to publication of the guidelines. However, a practitioner who employs an approach substantially different from these guidelines is advised to document in the patient record information sufficient to explain the approach taken.

The practice of medicine involves not only the science, but also the art of dealing with the prevention, diagnosis, alleviation, and treatment of disease. The variety and complexity of human conditions make it impossible to always reach the most appropriate diagnosis or to predict with certainty a particular response to treatment. Therefore, it should be recognized that adherence to these guidelines will not assure an accurate diagnosis or a successful outcome. All that should be expected is that the practitioner will follow a reasonable course of action based on current knowledge, available resources, and the needs of the patient to deliver effective and safe medical care. The sole purpose of these guidelines is to assist practitioners in achieving this objective.

I. INTRODUCTION

Examination of the colon by CT colonography is a useful procedure for evaluating the colon and is an evolving technology. It may be the initial method of colonic investigation or may be employed as an alternative to colonoscopy when the latter is contraindicated or imposes a significant medical risk, such as in patients on anticoagulation therapy or for whom sedation presents an increased risk. The goal of this radiologic examination is to establish the presence or absence of colorectal neoplasia by producing the optimum quality study at the minimum radiation dose necessary. This guideline is for the performance of CT colonography in adult patients.

Individuals undergoing this examination may fall into one of several risk populations, and the examination may be designated as screening, surveillance, or diagnostic. There are several evidence-based guidelines which, with minor variations, categorize individuals into specific risk groups with correlated recommendations for management. Screening identifies individuals who are more likely to have colorectal cancer or adenomatous polyps from among those without signs or symptoms of the disease. Based on age related risk, all individuals without other

risk factors who are 50 years or older are considered at average risk. Those with a single first-degree relative (mother, father, sister, brother, or child) who have had colorectal neoplasia before age 60 or multiple first-degree relatives with neoplasia diagnosed at any age are defined as at increased or above average risk. Individuals with a long-standing history of inflammatory bowel disease or from families with defined genetic syndromes are at high risk. Surveillance involves the ongoing monitoring of people with previously diagnosed colorectal neoplasm or inflammatory bowel disease. The degree of risk may be related to the underlying or prior pathology. Diagnostic examinations are performed on symptomatic individuals or as a follow-up to a prior but less definitive screening study. These individuals, by definition, are considered at greater risk to harbor colorectal neoplasia.

II. INDICATIONS

The indications for a CT colonography examination include, but are not limited to:

1. Screening examination in individuals who are at average or elevated risk for colorectal carcinoma or who have a first-degree relative with a history of colorectal neoplasm.
2. Surveillance examination in patients with a history of previous colonic neoplasm, either benign or malignant.
3. Diagnostic examination in patients with known or prior colorectal carcinoma and in symptomatic patients including, but not limited to, those with abdominal pain, diarrhea, constipation, gastrointestinal bleeding, anemia, intestinal obstruction, and weight loss.
4. Following incomplete screening, surveillance, or diagnostic colonoscopy.
5. Patients who require colonoscopy while on anticoagulant therapy.

All imaging facilities should have policies and procedures to reasonably attempt to identify pregnant patients prior to the performance of any examinations involving ionizing radiation. If the patient is known to be pregnant, the potential radiation risk to the fetus and clinical benefits of the procedure should be considered before proceeding with the study. (1995, 2005 - ACR Resolution 1a)

III. QUALIFICATIONS AND RESPONSIBILITIES OF PERSONNEL

See the ACR Practice Guideline for Performing and Interpreting Diagnostic Computed Tomography (CT).

In addition, it is recommended that supervising and interpreting physicians should have reviewed at least 50 cases in one or more of the following formats:

1. Formal hands-on interactive training on CT colonography interpretation.
2. Supervision with a CT colonography-trained physician(s) acting as a double reader.
3. Correlation of CT colonography and endoscopy findings in patients who undergo both procedures.

Qualifications of the radiologic technologist should include familiarity with the technical requirements of CT colonography.

IV. SPECIFICATIONS OF THE EXAMINATION

The written or electronic request for CT colongraphy should provide sufficient information to demonstrate the medical necessity of the examination and allow for its proper performance and interpretation.

Documentation that satisfies medical necessity includes 1) signs and symptoms and/or 2) relevant history (including known diagnoses). Additional information regarding the specific reason for the examination or a provisional diagnosis would be helpful and may at times be needed to allow for the proper performance and interpretation of the examination.

The request for the examination must be originated by a physician or other appropriately licensed health care provider. The accompanying clinical information should be provided by a physician or other appropriately licensed health care provider familiar with the patient's clinical problem or question and consistent with the state scope of practice requirements. (2006 - ACR Resolution 35)

A. Quality Control

The following quality controls should be applied to all CT colonography examinations:

1. Colon cleansing and distention should be adequate for detection of polyps 1 cm or larger.
2. Efforts should be made to ensure an optimal examination and to resolve questionable radiographic findings in the colon before the patient leaves the facility. Focused additional imaging of the patient should be performed as necessary.
3. The following is suggested for a quality control program:
   a. Radiologic, endoscopic, and pathologic findings should be correlated whenever available.
   b. Detection rates for colorectal cancer and polyps of 1 cm or greater should be determined and periodically monitored. A prevalence of 3-10% for polyps of 1 cm or

greater should be expected. There should be an assessment of false positive rates for all reported polyps.

B. Colon Preparation

The preparation should consist of a combination of dietary restriction, hydration, osmotic laxatives such as the saline cathartics, and contact laxatives. The intent is to achieve a colon that is free of fecal material and excess fluid or as close to this ideal as possible. Polyethylene glycol lavage solution may be used, although it may leave excess residual fluid in the colon.

There is insufficient evidence to recommend the routine use of oral contrast for labeling stool and/or fluid. In addition, "prepless" or "minimal prep" approaches have not been validated in clinical trials.

C. Examination Technique

1. An appropriate medical history should be available.
2. The patient should evacuate prior to insertion of the rectal tube.
3. The rectal tube tip should be inserted by a physician or a trained assistant (radiologic technologist, nurse, or physician assistant). If a rectal retention balloon is employed, inflation should be discontinued if the patient complains of pain. This may indicate an increased risk of perforation.
4. An antispasmodic agent such as glucagon may be administered to relieve significant spasm or patient discomfort.
5. A sufficient volume of room air or carbon dioxide should be manually or electronically administered to provide full colon distention.
6. The adequacy of colon distention should be checked with a scout image to ensure a complete and full column of gas throughout the colon before each CT acquisition.
7. Complete anatomic imaging of the colon and rectum should be obtained in both the supine and prone positions. Additional insufflation will usually be necessary.
8. Screening studies should be performed using a low-dose, nonenhanced CT technique. Generally this requires kVp=120, and mAs ≤ 100. Doses as low as 10 mAs have been shown to be adequate for primary 2D interpretation, but primary 3D evaluation may require 50-100 mAs. Patients with a large body habitus or metallic implants may require a higher dose for optimal imaging. Diagnostic examinations should be performed with intravenous contrast media administration, when not contraindicated, using standard body CT settings (kVp=120, mAs >200). Diagnostic studies are associated with an increased probability of colorectal carcinoma, which can be simultaneously staged, and an increased prevalence of extracolonic abnormalities, which can be better characterized and may represent the source of the symptom.
9. CT colonography is optimally performed on a multidetector CT (MDCT) scanner. Slice collimation of ≤ 3 mm with a reconstruction interval of ≤ 1.5 mm is optimal. The breathhold should not exceed 25 seconds. A maximum of 5 mm slice collimation with 2.5 mm reconstruction intervals is acceptable.
10. Networking capability should be available to transfer the image data to a workstation with specialized software for CT colonography interpretation.
11. The quality controls specific to the CT colonography study are:
    a. Complete anatomic coverage of the colon and rectum.
    b. Adequate colon distention and overall image quality. Each segment of the colon should be distended and free of most fluid and stool in at least one position. Suboptimally visualized colon should be scanned again. The use of decubitus views may be helpful in cases of suboptimal distention and excessive fluid.

D. Data Interpretation

The purpose of CT colonography is to accurately evaluate the colon for the presence or absence of clinically significant neoplastic lesions. Abnormalities may range from discrete mucosal elevations (which may be malignant or at risk to become malignant) to infiltrating tumors. Polyps should be measured in at least two planes utilizing multiplanar reconstruction and/or 3D images, and an assessment of the size of the lesion should be made based on the largest diameter. Lesion morphology (sessile, pedunculated, flat) and segmental location should be reported.

1. Colon Imaging

   CT data should be interpreted on a computer workstation that allows simultaneous axial imaging, multiplanar reformatted imaging, and 3D endoluminal viewing. Workstations should have the capability of displaying both axial supine and prone data together, and should allow the window width and level to be rapidly changed. Either a primary 2D interpretation technique using a cine function and scrolling through the axial images with a "colon tracking" technique or a primary 3D

endoluminal approach can be used for interpretation.

a. Primary 2D approach
Using colon tracking, the axial images are reviewed systematically at lung and soft tissue window settings using a cine function (scrolling). The colon is followed in its entirety from the ano-rectal verge to the cecum, and a search for polypoid intraluminal protrusions and assessment for abnormal wall thickness are performed.
   i. If an abnormality is suspected during the axial review, it should be interrogated with multiplanar reconstruction (MPR) and endoluminal views to evaluate the morphology of the suspected lesion.
   ii. Supine and prone data should be evaluated to determine if the lesion is mobile. Causes of mobility include residual fecal material, pedunculated polyp, or a colon segment on a long mesentery.
   iii. The window setting should be adjusted to determine if the lesion shows homogeneous soft tissue attenuation or is heterogeneous.

b. Primary 3D approach
An alternative approach to data interpretation is to perform 3D endoluminal imaging. To ensure complete visualization of the colonic surface, viewing should include antegrade (cecum to rectum) and retrograde (rectum to cecum) "fly throughs" using both supine and prone acquisitions. If an abnormality with morphologic characteristics of a polyp (round, oval, or lobulated) is detected on endoluminal imaging, it should be interrogated using 2D images to determine its attenuation characteristics and apparent mobility. Not all systems software is capable of providing adequate quality reconstructions for primary 3D interpretation. A determination should be made as to whether the system being used is appropriate for this approach.

2. Extracolonic Findings

Significant visualized extracolonic abnormalities should be documented. A study optimized for evaluation of colon abnormalities may not be optimal for extracolonic abnormalities.

V. DOCUMENTATION AND COMMUNICATION OF RESULTS

Reporting should be in accordance with the ACR Practice Guideline for Communication of Diagnostic Imaging Findings.

Any segment not adequately evaluated should be documented. All large masses and lesions that compromise luminal caliber should be communicated. Polyps ≥ 10 mm should be identified and described. Recommendations for endoscopic examination and their removal should be incorporated into the report.

Reporting of polyps ≤ 5 mm is not recommended. They are frequently non-neoplastic or, if adenomatous, have an extremely low malignant potential or probability of containing invasive cancer. Furthermore, a high percentage of polyps identified on CT colonography in this size range remain undocumented on subsequent colonoscopy, either because they represent false positive interpretations or as a result of the approximately 25% failure rate of colonoscopy to identify such lesions when present. The potential harm of colonoscopy may outweigh the benefits.

The reporting and recommendations for polyps measuring 6-9 mm may vary, depending on the certainty of the finding and clinical context. When identified with reasonable probability they should be reported. The likelihood that a polyp in this size category will progress to a clinically significant neoplasm diminishes with increasing patient age due to the low likelihood of malignant degeneration in conjunction with the long natural history of this process. In some individuals follow-up CT colonography at 3-5 years may be acceptable. Recommendations should be based upon consideration of the lesion size, diagnostic confidence, patient's age, and existing comorbid conditions. As the polyp approximates the upper limit of this size threshold, greater emphasis may be placed upon removal if the quality of the colonic preparation is adequate. It might be more appropriate to recommend polypectomy for a high probability polyp measuring 8-9 mm in an individual < 70 years of age.

Abnormalities or questionable abnormalities in structures unrelated to the colon may be identified during the process of reviewing the unenhanced 2D axial images of the colon. These are most common in, but not limited to, the kidneys, liver, adrenal glands, visualized portions of the lungs, and the major vessels. Characterization of extracolonic organs may be suboptimal with CT colonography technique. Likewise, extracolonic lesions may be present but not detectable. Most extracolonic findings are not clinically significant, and reporting may cause unnecessary patient anxiety and additional

diagnostic examinations. Clinical judgment should be used in reporting suspected extracolonic abnormalities.

VI. EQUIPMENT SPECIFICATIONS

Optimally, examinations should be performed with MDCT equipment meeting all applicable federal and state radiation standards as well as the requirements described in Section IV.C.

Equipment should provide diagnostic image quality and networking capability. Equipment should be capable of producing kilovoltage of 120 kVp or greater and ≤ 100 mAs.

VII. RADIATION SAFETY IN IMAGING

Radiologists, medical physicists, radiologic technologists, and all supervising physicians have a responsibility to minimize radiation dose to individual patients, to staff, and to society as a whole, while maintaining the necessary diagnostic image quality. This is the concept "As Low As Reasonably Achievable (ALARA)".

Facilities, in consultation with the medical physicist, should have in place and should adhere to policies and procedures, in accordance with ALARA, to vary examination protocols to take into account patient body habitus, such as height and/or weight, body mass index or lateral width. The dose reduction devices that are available on imaging equipment should be active or manual techniques should be used to moderate the exposure while maintaining the necessary diagnostic image quality. Patient radiation doses should be periodically measured by a medical physicist in accordance with the appropriate ACR Technical Standard. (2006 - ACR Resolution 17)

VIII. QUALITY CONTROL AND IMPROVEMENT, SAFETY, INFECTION CONTROL, AND PATIENT EDUCATION CONCERNS

Policies and procedures related to quality, patient education, infection control, and safety should be developed and implemented in accordance with the ACR Policy on Quality Control and Improvement, Safety, Infection Control, and Patient Education Concerns appearing elsewhere in the ACR Practice Guidelines and Technical Standards book.

For specific issues regarding CT quality control, see the ACR Practice Guideline for Performing and Interpreting Computed Tomography (CT).

Equipment performance monitoring should be in accordance with the ACR Technical Standard for Medical Physics Performance Monitoring of Computed Tomography (CT) Equipment.

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REFERENCES

1. Dachman AH, Glick S, Yoshida H. Computed tomography colonography and colon cancer screening. *Semin Roentgenol* 2003;38:54-64.
2. Gluecker T, Johnson CD, Wilson LA, et al. Extracolonic findings at CT colonography: evaluation of prevalence and cost in a screening population. *Gastroenterology* 2003;124:911-916.
3. Iannaccone R, Laghi A, Catalano C, et al. Detection of colorectal lesions: lower-dose multi-detector row helical CT colonography compared with conventional colonoscopy. *Radiology* 2003;229:775-781.

4. Johnson CD, Harmsen WS, Wilson LA, et al. Prospective blinded evaluation of computed tomographic colonography for screen detection of colorectal polyps. *Gastroenterology* 2003;125:311-319.
5. Macari M, Bini EJ, Jacobs SL, et al. Filling defects at CT colonography: pseudo- and diminutive lesions (the good), polyps (the bad), flat lesions, masses, and carcinomas (the ugly). *Radiographics* 2003;23:1073-1091.
6. Macari M, Bini EJ, Jacobs SL, et al. Colorectal polyps and cancers in asymptomatic average-risk patients: evaluation with CT colonography. *Radiology* 2004;230:629-636.
7. Pickhardt PJ, Choi JR, Hwang I, et al. Computed tomographic virtual colonoscopy to screen for colorectal neoplasia in asymptomatic adults. *N Engl J Med* 2003;349:2191-2200.
8. Pickhardt PJ, Choi JR, Nugent PA, et al. Flat lesions at virtual and optical colonoscopy: prevalence, histology, and sensitivity for detection in an asymptomatic screening population. *AJR* 2004;182:74-75.
9. Taylor SA, Halligan S, Burling D, et al. CT colonography: effect of experience and training on reader performance. *Eur Radiol* 2004;14:1025-1033.
10. Yee J, Kumar NN, Hung RK, et al. Comparison of supine and prone scanning separately and in combination at CT colonography. *Radiology* 2003;226:653-661.

Clinical Update
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Commentary: Colon-cancer screening has been endorsed by numerous medical professional societies, and several screening methods are reimbursable by most third-party payers. Of the screening methods, colonoscopy has the best sensitivity for polyps, with the added advantage of a therapeutic option during the initial examination, making it the currently favored method. There has been substantial press coverage of this important preventive health measure, and it has been incorporated into quality measures for primary care providers. Despite these facts, current compliance with any colon-cancer screening modality is only 30% to 40%. CT colonography (CTC) is a new, alternative method for imaging the colon. Drs Banerjee and Van Dam review the current methodology and the accuracy of CTC. They also review the cost and patient satisfaction issues that will help determine its ultimate role in colon imaging and colon cancer screening. – Grace H. Elta, MD

CT COLONOGRAPHY

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Colorectal cancer is the second leading cause of cancer death in the United States, claiming over 50,000 American lives annually. More than 130,000 new cases are diagnosed each year. The vast majority of colon cancers arise from readily identifiable precursor lesions, namely, adenomatous polyps in the colon. Screening for colorectal cancer in asymptomatic individuals, with detection and removal of these precursor lesions, can be expected to significantly impact the death rate from this largely preventable cancer.

The most used screening tests in the past decade have included some combination of fecal occult blood testing, sigmoidoscopy, or barium enema. New data from large studies published at the start of this millennium indicate that screening with flexible sigmoidoscopy missed more than 50% of proximal neoplastic colonic lesions.[1,2] This has led to a widespread consensus among gastroenterologists that complete colonic examination with colonoscopy is the most effective and desirable screening option. In addition to being the most effective test in detecting colonic polyps, colonoscopy also offers the singular advantage of allowing both detection and removal of polyps during the same procedure.

CTC is a new imaging modality, which is evolving as a possible alternative to colonoscopy for colon-cancer screening. In this review, we describe the technique and examine the currently available data on the efficacy of CTC for colorectal-cancer screening.

TECHNIQUE

At this time, bowel preparation similar to that necessary for colonoscopy is also required for CTC. This is typically a polyethlyethylene glycol solution alone or in combination with magnesium citrate or bisacodyl. In addition, some centers have used oral contrast agents to label residual stool and colonic fluid to improve diagnostic accuracy. Image processing software that electronically removes the opacified residual colonic fluid from CT images has also been used to improve diagnostic accuracy.

A rectal tube is inserted, and room air or carbon dioxide is insufflated into the patient's colon to the point of patient discomfort. CT images are then acquired with the patient in both prone and supine positions, with the best results reported when using multidetector (4 or 8 channel) CT scanners, which allow for rapid image acquisition and superior image resolution. Standard helical images of the colon are then manipulated by imaging software to produce 2-dimensional axial images. In addition, 3-dimensional rendered views of the colon, which simulate endoluminal views obtained during colonoscopy, can be reproduced.

SAFETY OF CTC

The surface radiation dose received during CTC is approximately 0.44 rem, roughly equivalent to undergoing two abdominal films. This is a relatively

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TABLE 1. RECENT MULTICENTER STUDIES USING MULTIDETECTOR SCANNERS, COMPARING CTC WITH COLONOSCOPY

Study	Subjects (n)	Population Studied	Per Polyp Sensitivity		Per Patient Sensitivity		Per Patient Specificity	
			M: 6-9 mm	L: ≥10 mm	M: 6-9 mm	L: ≥10 mm	M: 6-9 mm	L: ≥10 mm
Pickhardt et al[5] (2003)	1233	Average risk*	86%	92%	89%	94%	80%	96%
Cotton et al[6] (2004)	615	Increased risk	23%	52%	30%	55%	93%	96%
Rockey et al[7] (2005)	614	Increased risk*†‡§	47%	53%	51%	59%	89% (≥ 6 mm)	96%

M, medium size; *L*, large size.
*Family history of colon cancer.
†Positive fecal occult blood.
‡Hematochezia.
§iron deficiency anemia.

small dose of radiation. However, if a strategy of surveillance with repeat CTC at short intervals is used for patients with small polyps, cumulative radiation exposure over years may become a matter of concern.

Two cases of perforation have now been described in patients who underwent virtual colonoscopy.[3,4] Both were felt to have arisen as a consequence of overinflation with air in patients with diseased colons.

FALSE-NEGATIVES AND FALSE-POSITIVES ON CTC

Typical reasons for false-positives on CTC have included stool in the colon, breath-hold artifacts, and protruding haustral folds in poorly distended colonic segments, all of which mimic polyps. Inadequate bowel cleansing and inadequate colonic distension increase the probability of both false-positives and false-negatives. Combining 2-dimensional and 3-dimensional views decreases the chances of misdiagnosing polyps. The rectum and the sigmoid colon remain problematic areas in interpreting CTC, the latter particularly in patients with severe diverticulosis.

Perceptual failure, where the polyp is evident on the CTC but is not recognized as such by the reader, accounts for over half of the errors in several studies. The major factors in perceptual failure are probably inadequate training, because reading a CTC has a steep learning curve, and reader fatigue caused by reading an overly high volume of cases.

STUDIES COMPARING CTC WITH COLONOSCOPY

Although several studies have been performed comparing CTC with colonoscopy,[3] recently published large multicenter studies that used multidetector scanners are of particular interest and best reflect the disparate state of the evolution of CTC at present (Table 1).[5-7] The best results were reported by Pickhardt et al5 who essentially reported similar sensitivities for CTC and colonoscopy in the detection of medium-sized and large polyps. The superior results noted in this study may be explained by a combination of the following factors. Careful bowel preparation with sodium phosphate and bisacodyl was performed to minimize bowel fluid and confounding artifacts. Barium was used to achieve solid-stool tagging and opacification of colonic fluid achieved with Gastrografin (Bracco Diagnostics, Princeton, NJ). It is unclear if the presence of barium and Gastrografin in the colon adversely affected the performance of colonoscopy in this study. Multidetector scanners were used, which permitted faster and higher-resolution imaging. "Electronic cleansing" was achieved by using software that digitally removed any opacified residual colonic fluid from CT images. Finally, primary readings were performed by using 3-dimensional imaging, with 2-dimensional images used only for problem solving. This approach most closely simulates conventional colonoscopy. For all adenomatous polyps ≥ 6 mm, the per polyp sensitivities were 86% and 90% for CTC and colonoscopy, respectively. For adenomatous polyps ≥ 10 mm, the sensitivities were 92% and 88% for CTC and colonoscopy, respectively. When the CTC data were analyzed on a per patient basis, the sensitivity and the specificity for polyps > 6 mm were 88% and 80%, respectively, and those for polyps > 10 mm were 94% and 96%, respectively. These data suggest that, with optimal bowel preparation, the use of multidetector CT scanners and image processing that allows for electronic cleansing, the effects of perceptual failure in CTC readers can be minimized, allowing CTC to approximate the accuracy of colonoscopy.

The subsequent 2 recent studies may reflect the reality of the future performance of CTC when transferred out of academic centers with a special interest in the technology to multiple centers, including community settings, with less well-trained readers or with readers who do not have a special passion for the technology.

Cotton et al[6] studied 600 symptomatic patients or patients with a history of polyps at 9 major academic institutions by using 2- and 4-section scanners.[6] Conventional colonoscopy detected 99% of lesions 6 to 9 mm in size and 96% of lesions ≥ 10 mm, compared with only 23% and 52% of lesions for CTC. The poor results in this study may reflect the limited experience of radiologists in 8 of the 9 centers, because the radiologists who read the CTCs were only required to have performed 10 prior procedures. In contrast, the radiologists in the study reported by Pickhardt et al[5] were required to have trained by reading at least 25 prior CTCs, and 2 radiologists had read over 100 studies. Oral contrast and "electronic cleansing" were not used by Cotton et al.[6] Again, CTC was read in the 2-dimensional mode, with 3-dimensional readings limited to problem solving. This mode of reading may have impacted on the final results to a limited extent.

Similar disappointing results were recently described by Rockey et al,[7] despite the use of superior CT scanners and the participation of more experienced and better trained CTC readers than those used by Cotton et al.[6] In this multicenter study, 614 subjects at increased risk underwent 4- and 8-slice multidetector scanning. Images were interpreted by primary 2-dimensional

reading, with 3-dimensional readings for problem solving. For lesions ≥ 10 mm, per lesion sensitivity for colonoscopy was 99% compared with 53% for CTC. For lesions 6 to 9 mm in size, the sensitivity of colonoscopy was again 99% compared with only 47% for CTC. Approximately half the CTC readers had prior experience of reading more than 50 cases. CTC readers with less experience were required to complete a CTC training module. A greater prior experience in reading CTC did not result in a higher detection rate for polyps. Indeed, readers with less prior experience detected more lesions of all sizes than more experienced readers. This may be a result of the fact that they were required to complete formal training.

PROBLEMATICAL LESIONS FOR CTC: SMALL OR FLAT POLYPS

Increasing polyp size results in an increasing risk of cancer. About 1% of polyps > 10 mm in size become cancers per year. Similarly, about 2% to 7% of adenomas in the 6- to 9-mm range will have areas of high-grade dysplasia, and close to 1% will harbor invasive cancer. Colonoscopic removal of polyps in these size ranges is clearly desirable and uncontroversial.

CTC has been shown in several studies to have poor sensitivity and specificity for polyps ≤ 5 mm. The risk of cancer is considerably less than 1% in polyps in this size range and may be as low as 0.25% for polyps in this size range. It has been suggested that the poor sensitivity of CTC in this size range is less important given the lower neoplastic potential of polyps in this size group.

The problem may, in fact, prove to be determining a satisfactory course of action in patients where CTC does detect a small polyp (≤ 5 mm). Up to 45% of screened patients aged ≥ 50 years will have small polyps, and many of these polyps will be detected at CTC. Referral of all patients with small polyps for subsequent colonoscopy will have a negative impact on the cost-effectiveness of CTC as a primary screening modality. It has been suggested that these patients simply be followed by CTC at shorter intervals, without referral for colonoscopic removal. This too will negatively impact on the cost-effectiveness of CTC. In addition, this strategy will probably increase patient risks for colon cancer and will expose patients to cumulative doses of ionizing radiation. This passive strategy may also prove unacceptable to patients and their physicians, particularly in the absence of data regarding its safety.

CTC IN PATIENTS WITH AN INCOMPLETE COLONOSCOPY

Colonoscopy cannot be completed in approximately 5% of patients for technical reasons, including bowel tortuosity or fixity, or because of a stenosing lesion. Although a barium enema is typically obtained to complete visualization of the proximal colon in these patients, it is known that the sensitivity of double-contrast barium enema (DCBE) for the detection of polyps is poor, with a detection rate of only 44% for polyps > 10 mm.[8] CTC appears superior to a barium enema for polyp detection. In a large study of 837 asymptomatic persons at above-average risk for colorectal cancer, CTC readers detected 56% to 79% of polyps ≥ 10 mm in diameter, compared with the detection of only 39% to 56% of these polyps when using DCBE.[9]

Superior results with CTC were confirmed by Rockey et al[7] in a further large (n = 614) multicenter study,[7] where CTC detected significantly higher numbers of polyps than DCBE for both medium-size (6-9 mm) lesions (47% vs. 30%) and large (≥ 10 mm) lesions (53% vs. 45%). In addition, CTC is better tolerated than DCBE.[10] CTC, therefore, would appear to be the preferable imaging modality in patients with an incomplete colonoscopy, where visualization of the proximal colon is desirable.

EXTRACOLONIC FINDINGS

A further possible advantage of CTC is its concurrent ability to image and detect additional unsuspected abnormalities in extracolonic abdominal tissues. Extracolonic abnormalities considered highly significant have been found in 10% to 23% of subjects imaged, moderately significant in 27% to 52%, and with abnormalities of low significance occurring in up to 50% of imaged patients.[11,12] However, these detected extracolonic abnormalities will require further physician consultations and diagnostic testing and will, therefore, add to the incremental costs of the screening program. While lives will undoubtedly be saved by the detection of additional unsuspected abdominal pathology at CTC, many unnecessary diagnostic tests, including tests with the potential for complications, will also be performed for what will eventually be determined to be medical unimportant findings. In addition, the reading time and, hence, the costs of CTC will also increase if reading for extracolonic findings is determined to be an essential part of the examination. Conversely, limiting the reading and the reporting to colonography alone would raise ethical and legal issues.

COST-EFFECTIVENESS OF CTC

At current prices, standard colonoscopy appears to be more cost effective than CTC. By using Markov modeling, screening by CTC was determined to cost $24,586 per life-year saved, compared with $20,930 for colonoscopic screening. Screening by colonoscopy was found to remain more cost effective, even assuming a sensitivity and a specificity for CTC of 100%. To achieve cost-effectiveness similar to colonoscopy, CTC needed to have an initial compliance rate of 15% to 20% better than colonoscopy or to cost 54% less.[13]

PATIENT PREFERENCE

It is unclear if patients find CTC preferable to colonoscopy. In the two largest (n > 600) studies, subjects experienced similar levels of discomfort with either procedure[14] or expressed no preference for either procedure.[6] Bowel preparation was perceived as the worst part of both procedures. Developments in stool-tagging techniques, permitting "prepless" CTC,[15,16] could result in patient preferences swinging in its favor.

Although colonoscopy is perceived as being more invasive than CTC, if patients are told that they may have a 20% or greater chance of having a polyp detected at CTC that will require repeat bowel preparation followed by colonoscopy, then many might prefer to go directly to colonoscopy. Similarly, if they are told that a small polyp may be noted at CTC, which will then require surveillance over several years with repeated CTCs, then direct colonoscopy would be more appealing to many. Colonoscopy offers the clear advantage of one-stop diagnosis and therapy, obviating the protracted anxiety that might arise from having a "small" polyp, which is followed without removal for years. Finally, newer colonoscopic construction designs may obviate or diminish the discomfort associated with colonoscopy and, hence, the need for sedation, while simultaneously minimizing complication rates.

UPCOMING ADVANCES IN CTC

The more immediate advances will include increasing use of multidetector row CT scanners, which will allow higher-resolution images with shorter breath holds. Improvements in software will result in improved image manipulation, allowing 3-dimensional retrograde as well as anterograde fly throughs, which should improve the colonic surface area visualized and improve sensitivity. Software improvements have recently allowed "digital cleansing" of residual stool and colonic fluid that previously have been opacified with oral contrast, allowing for increased diagnostic accuracy.[5] Reader-associated perceptual errors may be minimized with the ongoing development of software for computer-aided detection of lesions. Stool-tagging techniques are likely to evolve and may eventually allow for "prep-less" CTC.[15,16]

REFERENCES

1. Imperiale TF, Wagner DR, Lin CY, Larkin GN, Rogge JD, Ransohoff DF. Risk of advanced proximal neoplasms in asymptomatic adults according to the distal colorectal findings. N Engl J Med. 2000;343:169-174.
2. Lieberman DA, Weiss DG, Bond JH, Ahnen DJ, Garewal H, Chejfec G. Use of colonoscopy to screen asymptomatic adults for colorectal cancer. Veterans Affairs Cooperative Study Group 380. N Engl J Med. 2000;343:162-168.
3. Kamar M, Portnoy O, Bar-Dayan A, et al. Actual colonic perforation in virtual colonoscopy: report of a case. Dis Colon Rectum. 2004;47:1242-1244.
4. Coady-Fariborzian L, Angel LP, Procaccino JA. Perforated colon secondary to virtual colonoscopy: report of a case. Dis Colon Rectum. 2004;47:1247-1249.
5. Pickhardt PJ, Choi JR, Hwang I, et al. Computed tomographic virtual colonoscopy to screen for colorectal neoplasia in asymptomatic adults. N Engl J Med. 2003;349:2191-2200.
6. Cotton PB, Durkalski VL, Pineau BC, et al. Computed tomographic colonography (virtual colonoscopy): a multicenter comparison with standard colonoscopy for detection of colorectal neoplasia. JAMA. 2004;291:1713-1719.
7. Rockey DC, Paulson E, Niedzwiecki D, et al. Analysis of air contrast barium enema, computed tomographic colonography, and colonoscopy: prospective comparison. Lancet. 2005;365:305-311.
8. Ott DJ. Analysis of Accuracy, Complications and Cost of Barium Enema for CRC Diagnosis. Bethesda, MD: National Institutes of Health; 1994.
9. Johnson CD, MacCarty RL, Welch TJ, et al. Comparison of the relative sensitivity of CT colonography and double-contrast barium enema for screen detection of colorectal polyps. Clin Gastroenterol Hepatol. 2004;2:314-321.
10. Morrin MM, Kruskal JB, Farrell RJ, Goldberg SN, McGee JB, Raptopoulos V. Endoluminal CT colonography after an incomplete endoscopic colonoscopy. AJR Am J Roentgenol. 1999;172:913-918.
11. Hara AK, Johnson CD, MacCarty RL, Welch TJ. Incidental extracolonic findings at CT colonography. Radiology. 2000;215:353-357.
12. Gluecker TM, Johnson CD, Wilson LA, et al. Extracolonic findings at CT colonography: evaluation of prevalence and cost in a screening population. Gastroenterology. 2003;124:911-916.
13. Sonnenberg A, Delco F, Bauerfeind P. Is virtual colonoscopy a cost-effective option to screen for colorectal cancer? Am J Gastroenterol. 1999;94:2268-2274.
14. Gluecker TM, Johnson CD, Harmsen WS, et al. Colorectal cancer screening with CT colonography, colonoscopy, and double-contrast barium enema examination: prospective assessment of patient perceptions and preferences. Radiology. 2003;227:378-384.
15. Bielen D, Thomeer M, Vanbeckevoort D, et al. Dry preparation for virtual CT colonography with fecal tagging using water-soluble contrast medium: initial results. Eur Radiol. 2003;13:453-458.
16. Iannaccone R, Laghi A, Catalano C, et al. Computed tomographic colonography without cathartic preparation for the detection of colorectal polyps. Gastroenterology. 2004;127:1300-1311.

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