February 5, 2014

Virginia A. Moyer, MD, MPH
Chair
United States Preventive Services Task Force
540 Gaither Road
Rockville, MD  20850

RE: United States Preventive Services Task Force Draft Research Plan for Colorectal Cancer Screening

Dear Dr. Moyer,

The American College of Gastroenterology (ACG) appreciates the opportunity to offer comments in response to the United States Preventive Services Task Force’s (USPSTF) recently announced review of its recommendations on colorectal cancer screening.

The ACG is a physician organization representing gastroenterologists and other gastrointestinal specialists. Founded in 1932, our organization currently includes over 13,000 physicians among its membership of health care providers of gastroenterology specialty care and we focus on the issues confronting the gastrointestinal specialist in treatment of patients. The primary activities of ACG have been, and continue to be, promoting evidence-based medicine and optimizing quality of patient care.

BACKGROUND

Colorectal Cancer Prevention Tests vs. Colorectal Cancer Detection Tests

The ACG agrees with other organizations and interested stakeholders in dividing the various screening modalities into “colorectal cancer prevention” versus “colorectal cancer detection.” In 2008, the ACG was an integral part of the U.S. Multi Society Task Force (MSTF) on Colorectal Cancer Screening,1 together with the American Cancer Society and the American College of Radiology, which concluded that colorectal cancer prevention is the preferred strategy and primary goal over colorectal cancer detection.2 These tests include tests that are designed to detect both early cancer and adenomatous polyps.

The ACG’s guideline on colorectal cancer screening also divide tests into cancer prevention versus detection tests, in recommending the preferred cancer prevention test (colonoscopy every

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1 "U.S. Multi-Society Task Force on Colorectal Cancer": the American College of Gastroenterology, the American Gastroenterological Associations, and the American Society for Gastrointestinal Endoscopy
10 years) and a preferred cancer detection test (annual fecal immunochemical test (FIT)) to detect occult bleeding.  

The ACG recommends the USPSTF to also stipulate between screening tests that detect colorectal cancer versus tests that help prevent colorectal cancer. This is important when rating various screening modalities, but also because private and public health insurance programs use USPSTF recommendations in insurance coverage and patient cost-sharing policies. The USPSTF website recognizes its role in helping to set national coverage determinations pursuant to federal law, such as the Patient Protection and Affordable Care Act (or “ACA”). One of the reasons why colorectal cancer prevention tests such as optical colonoscopy or sigmoidoscopy have an “A” USPSTF rating is because the screening and therapeutic intervention occurs during the same procedure. The ACG urges the USPSTF to clearly stipulate in its updated recommendations that the therapeutic portion of a colorectal cancer screening (polyp removal) is integral to the screening examination itself. This stipulation would serve two purposes: it would help the USPSTF to compare various colorectal cancer screening modalities when updating recommendations and it would also rectify insurance coverage and patient cost-sharing quirks related to those colorectal cancer screenings turning into therapeutic procedures (polyp removal). Under current Medicare law, pursuant to the ACA, a colorectal cancer screening recommended by the USPSTF would come with no out-of-pocket cost to the Medicare beneficiary, yet when a polyp is found and removed -- the whole purpose if the screening examination itself -- the very same procedure is coded differently no longer considered a “screening” for Medicare coverage and beneficiary cost-sharing purposes. 

American College of Gastroenterology’s Colorectal Cancer Screening Guidelines
The ACG recommends complete, optical colonoscopy as the preferred method used to screen asymptomatic patients for colon cancer as the procedures examines the entire colon and allows for simultaneous therapeutic intervention.

The most recent version of the American College of Gastroenterology Guidelines for Colorectal Cancer Screening states:

<table>
<thead>
<tr>
<th>Preferred Cancer Screening Modalities</th>
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<tr>
<td><strong>Cancer prevention tests should be offered first. The preferred prevention test is colonoscopy every 10 years, beginning at age 50. Screening should begin at age 45 years in African Americans</strong></td>
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<tr>
<td><strong>Cancer detection test. This test should be offered to patients who decline colonoscopy or another cancer prevention test. The preferred cancer detection test is annual FIT for blood</strong></td>
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4 [http://www.uspreventiveservicestaskforce.org/uspsf/uspsabrecs.htm](http://www.uspreventiveservicestaskforce.org/uspsf/uspsabrecs.htm)

DISCUSSION

Rationale for a “preferred” strategy
The ACG recommends that clinicians have access to a “preferred” strategy for making colorectal cancer (CRC) screening recommendations, as an alternative to the “menu of options” approach by the performance characteristics and effectiveness of each test. Consistent with the various organizations’ conclusion that colorectal cancer prevention is the goal, ACG recommends colonoscopy every 10 years based on the evidence of colonoscopy effectiveness, cost-effectiveness, and acceptance by patients. The ACG also recommends FIT as the preferred colorectal cancer detection test. It should be noted that any positive finding as a result of a FIT test will require the patient to undergo optical colonoscopy.

A “preferred” strategy simplifies and clarifies discussions with patients and could also increase the likelihood that screening is offered to patients. One randomized trial showed that patients were more likely to undergo screening with the “preferred” strategy approach compared with the “menu of options.” Another study found no improvement in screening rates when multiple options were presented. Maintaining simplicity in guidelines may have value, in that patients may forgo the necessary follow-up diagnostic colonoscopy subsequent to a positive finding of another colorectal cancer prevention or detection test. However, the MSTF notes that patients may benefit from a set of options based on the needs of those individual patients, in consultation with their physician, and the technology available. The ACG also acknowledges that listing complete optical colonoscopy as a “preferred” CRC prevention strategy places greater emphasis on effectiveness than on risk or the ability to increase CRC screening utilization rates. Preferred screening modalities are not infallible and each have their limitations in access to care and increasing colorectal cancer screening utilization rates: While many describe optical colonoscopy as the “gold standard” in CRC screening, any discussion regarding a “gold standard” in colorectal cancer screening must not be misinterpreted as a “silver bullet” in preventing and eradicating colorectal cancer. The best test is the test that gets done. That said, the expert review of the medical literature supports ACG’s determination that there are preferred screening modalities when dividing colorectal cancer prevention versus colorectal cancer detection tests. What’s more, the MSTF concluded that complete optical

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7 Griffith JM, Lewis CL, Brenner AR et al. The effect of offering different numbers of colorectal cancer screening test options in a decision aid: a pilot randomized trial. BMC Med Inform Decis Mak 2008;8:4; Available at http://www.biomedcentral.com/1472-6947/8/4
colonoscopy is required to confirm positive findings in all other colorectal cancer prevention and detection tests (even flexible sigmoidoscopy).\(^9\)

**Complete Optical Colonoscopy**

There is a clear consensus that colorectal cancer prevention is the primary goal.\(^10\) Unlike other cancer screenings where early detection is the goal, screening with optical colonoscopy has the unique ability to prevent colorectal cancer by examining the entire colon and removing precancerous polyps during the same encounter. That is why the College believes that complete optical colonoscopy is the preferred standard in colorectal cancer prevention. New findings published in *The New England Journal of Medicine* (NEJM) in March 2012 highlight the ability to reduce colorectal cancer deaths through polyp detection and removal. This NEJM study reports a 53 percent reduction in colorectal cancer deaths following removal of adenomatous polyps during colonoscopy.\(^11\) This underscores the ACG position evident in the clinical guideline that colonoscopy remains the preferred colorectal cancer prevention strategy over all currently available options.\(^12\)

There is also now unequivocal evidence that serrated polyps may progress via the serrated neoplasia pathway to colorectal adenocarcinoma, and there are reasons to suspect that this pathway may contribute disproportionately to interval or missed cancers. The presence of large polyps (≥1 cm) is a risk factor for colorectal cancer, particularly colorectal cancer of the proximal colon.\(^13\) Recent reports of the serrated adenoma prevalence defined at screening colonoscopy have demonstrated this risk to be 4-13\%.\(^14\)\(^15\)

Furthermore, serrated cancers are common, likely accounting for 10-20% of all colorectal cancers and >30% of interval cancers.\(^16\) It is now recognized that up to 30% of colorectal cancers do not arise through conventional adenomas but rather through a serrated polyp pathway characterized by proximal colon location, hypermethylation and mutations in the BRAF oncogene.\(^17\) The predominant precancerous lesion in this pathway is the sessile serrated polyp (SSP). SSP is synonymous with sessile serrated adenoma but is commonly now called SSP because most of the lesions are not dysplastic. Hypermethylated cancers arising through this pathway are over-represented among cancers that develop after colonoscopy, and difficulty in detecting SSPs may be a major contributor to why colonoscopy is less effective in proximal colon cancer protection compared to distal cancer protection. SSPs have proven a challenge for endoscopists to detect

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9 A Joint Guideline from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology. Page 144.  
10 A Joint Guideline from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology. Page 133.  
12 American College of Gastroenterology guidelines for colorectal cancer screening 2009. Page 739  
13 Terdiman JP, McQuaid KR. Surveillance guidelines should be updated to recognize the importance of serrated polyps. Gastroenterology. 2010 Nov;139(5):1444-7  
because of their subtle appearance and an invariable sessile or flat morphology.\textsuperscript{18} The importance of early recognition and appropriate resection of these lesions is highlighted by a recent large, single-center study (1,189 patients), in which non-polypoid lesions were found in approximately 1 in every 11 individuals undergoing elective optical colonoscopy. The 170 non-polypoid/flat lesions they detected contained 15 cancers, nearly 10x the rate (odds ratio, 9.78; 95% CI, 3.93-1035).\textsuperscript{19}

The ACG requests that the USPSTF include serrated lesions as a data point in its systematic review of what are the test performance characteristics.

As noted above, optical colonoscopy has its limitations. As the MSTF consensus document and guidelines note, the patient’s commitment to bowel preparation and the physician’s skill in detecting potentially adenomatous polyps directly impact its effectiveness.\textsuperscript{20} Missed lesions and post-polypectomy bleeding are among the risks in colonoscopy. According to MSTF guidelines, colonoscopy had miss rates of 6-12% large adenomas and a 5% of cancers.\textsuperscript{21} Although extremely rare, optical colonoscopy brings a risk of perforation as well. Access to a setting performing colonoscopy and financial resources are also limitations. However, each of these limitations are also associated with other colorectal cancer prevention modalities and the USPSTF may not take access to care or costs into consideration when updating recommendations as well.

FIT
ACG guidelines conclude that the preferred cancer detection test is annual FIT. This is test has superior performance characteristics when compared with older guaiac-based Hemoccult II cards.\textsuperscript{22} There were 10 and 12 % gains in adherence with the FIT in randomized controlled trials comparing the FIT with guaiac-based testing, with overall results of superior performance and improved adherence in the detection of advanced lesions and little loss of positive predictive value.\textsuperscript{23}

ACG supports the recommendations that older guaiac-based fecal occult blood testing be abandoned as a method for CRC screening.\textsuperscript{24}

Other Effective Screening Modalities
ACG guidelines recognize that there are effective alternative colorectal cancer prevention and detection tests should the patient be unable or unwilling to undergo preferred screening modalities. Alternative colorectal cancer prevention tests include flexible sigmoidoscopy (every 5-10 years) and CT colonography (every 5 years). Alternative colorectal cancer detection modalities include annual Hemoccult Sensa and Fecal DNA testing (every 3 years). According to

\textsuperscript{18} AM J Gastroenterol 2012; 107: 1315-29.
\textsuperscript{19} Soetikno RM, Kaltenbach T, Rouse RV, Park W, Maheshwari A, Sato T, Matsui S, Friedland S. Prevalence of nonpolypoid (flat and depressed) colorectal neoplasms in asymptomatic and symptomatic adults JAMA. 2008 Mar 5;299(9):1027-35.
\textsuperscript{20} A Joint Guideline from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology.  Page 145
\textsuperscript{21} A Joint Guideline from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology.  Page 145
\textsuperscript{22} American College of Gastroenterology guidelines for colorectal cancer screening 2009.  Page 741
\textsuperscript{23} American College of Gastroenterology guidelines for colorectal cancer screening 2009.  Page 741
ACG guidelines, these alterative detection strategies play an important role in detection of colon cancer.  

**CT Colonography (CTC)**

CTC provides a time-efficient procedure with good accuracy and minimal invasiveness. No sedation or recovery time is required, nor is a chaperone needed to provide transportation after the procedure. Time permitting, patients can return to work on the same day. It is a common misperception, however, that bowel preparation is not required before undergoing CTC.

The accuracy of CTC is influenced by lesion size, and the sensitivity and specificity of CTC improves with polyp size. The accuracy of CTC in measuring polyp size is of particular importance since accurate size estimation is critical for appropriate patient management and for minimizing the false-positive rate. The principle performance feature that justifies inclusion of CT colonography as a viable alternative in ACG guidelines is that the sensitivity for larger polyps >=1 cm in size in the most recent multicenter U.S. trial was 90% (95% CI: 84%, 96%) and specificity 86% (95% CI: 81.3%, 90.0%). In other words, the ability of CT colonography to correctly identify an advanced polyp could be as low as 84% and its ability to correctly exclude patients with an advanced polyp as low as 86%. Accordingly, if using CTC criteria for referral of large polyps >9mm for colonoscopy, if at 0,5 and 10 yrs, 42% of patients without a large polyp would be referred for colonoscopy.

Second, the inability to detect polyps 5 mm and smaller, which constitutes 80% of colorectal neoplasms, and whose natural history is still not understood, necessitates performance of the test every 5 years, rather than 10-year intervals. Although management of polyps < 1 cm in size remains a topic for discussion for some non-specialists in the colon and rectum, the ACG continues to recommend that patients with polyps 6 mm or larger (detected by CT colonography) be referred for polypectomy, as should patients with three or more polyps of any size read with high confidence. Polyps <=5 mm in size interpreted with high confidence should be described in the CT colonography report. Unfortunately, false positives are common and the specificity for polyps >=1 cm in size in the National CT Colonography Trial was only 86%, with a positive predictive value (PPV) of 23%. The implications for this low PPV has significant cost implications.

Detection of flat lesions (including cancers) has been extremely variable and not well studied—particularly outside experienced centers of excellence. High miss rates for flat polyps and cancer have been evident and the sensitivity and optimal techniques of CT colonography for the detection of flat lesions have not yet been established. The extrapolation of even these variable findings (e.g. for detection of large polyps ≥ 1 cm sensitivity (90%) and specificity (86%) and PPV (23%)) to the general community of radiologists may represent a concern for patient safety.

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26 A Joint Guideline from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology. Page 149.
27 A Joint Guideline from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology. Page 150.
29 A Joint Guideline from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology. Page 150.
30 A Joint Guideline from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology. Page 150.
The ACG continues to stress the implications of repeated radiation emissions from CT colonography and other radiologic scans during routine screening procedures for asymptomatic patients. Medical research suggests that the harmful effects of radiation during routine screening procedures should be avoided and that the threshold risk for increased radiation related cancer is increased after one abdominal CT scan. As Johnson et al discussed, the FDA lists radiation derived from radiological sources as a known carcinogen, yet the U.S. Federal Government has not established guidelines for acceptable indications and radiation doses for CT scans. Recognizably, radiation exposure is cumulative and additive over the lifetime of the patient. The use of ionizing radiation for screening has been forbidden by law in several countries (for example: Germany and Switzerland).

**Flexible Sigmoidoscopy**
The ACG recommends flexible sigmoidoscopy every 5-10 years. Flexible sigmoidoscopy was associated with a 60% to 80% reduction in CRC mortality for the area of the colon within its reach, and this protective effect appears to persist for 10 years or more. The chief advantage of FSIG is that it can be performed with a simple preparation without sedation, and by a variety of examiners in diverse settings.

However, there is evidence that if a patient has an adenoma of any size in the distal colon, he or she has an increased risk of proximal advanced neoplasia (2-fold or higher) compared with patients who have no polyps or only hyperplastic polyps in the distal colon. Therefore, the MSTF recommends that most patients who have adenomas discovered at sigmoidoscopy should undergo colonoscopy. Patients should fully understand that in most circumstances colonoscopy will be recommended if an adenoma is detected during flexible sigmoidoscopy and that if they are unwilling to accept referral to colonoscopy, they should have a different form of screening.

**ACG Recommendations: Age to begin screening**
The ACG continues to recommend that screening begin at age 50 years in average-risk persons (i.e., those without a family history of colorectal neoplasia). ACG also recommends that screening begin at age 45 years in African Americans. The mean age of CRC development in African Americans is younger than that of other ethnicities. There is also evidence for a more proximal colonic distribution of cancers and adenomas in African Americans. African Americans are less likely to have undergone diagnostic testing and screening for colorectal cancer.

36 A Joint Guideline from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology. Page 141
37 A Joint Guideline from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology. Page 142
The “average risk” population is large and complex with regard to risk. Certain other subgroups of the average-risk population might warrant initiation of screening at an earlier or later age, depending on their risk. For example, the age-adjusted risk of incident cancers and prevalent adenomas is greater in men than in women. Pending further study and evaluation of this issue, the ACG recommends that screening begin at age 50 years for both the genders (at age 45 years for African-American men and women).

CONCLUSION

The ACG welcomes the opportunity to work with the USPSTF on developing CRC screening recommendations consistent with clinical guidelines and the currently available and appropriate evidence based medical literature. It is important that we work together to mitigate preventable CRC incidence rates and deaths. Please contact Brad Conway, Vice President of Public Policy, Coverage & Reimbursement at 301.263.9000 or bconway@gi.org to discuss further.