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Submitted Electronically

United States Preventive Services Task Force
Agency for Healthcare Research and Quality
540 Gaither Road
Rockville, MD 20850

**RE: United States Preventative Services Task Force Draft Recommendations for Colorectal Cancer Screening**

Dear Task Force Members:

The American College of Radiology (ACR), representing more than 40,000 diagnostic radiologists, interventional radiologists, radiation oncologists, nuclear medicine physicians, and medical physicists, appreciates the opportunity to comment on the United States Preventative Services Task Force's (USPSTF) draft recommendations for colorectal cancer screening. The ACR feels strongly that current evidence on the risks and benefits of Computed Tomography colonography (CTC) continue to show that CTC is proven to be an effective tool for screening of asymptomatic patients for colorectal cancer and should be a recommended screening test in all adults age 45 years and older. Significant peer-reviewed evidence on the efficacy of CTC has been and continues to be published regularly.

CTC is a valuable screening technology that can advance the goal of increasing colorectal cancer screening rates and reduce the mortality rate in colorectal cancer patients. There are more than 145,000 Americans diagnosed with colorectal cancer every year, and over 50,000 die because of late detection. Colorectal cancer is the third most common cancer diagnosed among men and women in the United States and the second overall leading cause of cancer death considering men and women together, despite having a 90 percent cure rate when detected early.

The ACR strongly supports the proposed USPSTF recommendation of a Grade A for colorectal cancer screening in adults ages 50 to 75 years and a Grade B for colorectal cancer screening in adults ages 45 to 49 years. Additionally, providing patients a variety of effective screening tools for colorectal cancer, including CTC, encourages early detection in the fight against this deadly disease and helps save lives as well as closing the gap in colorectal screening rates between whites and minority populations.

Additionally, the ACR proposes the following change to ensure full follow-up: "Under current ACA requirements, insurance providers required to cover Grade A and B recommendations without cost-sharing will need to cover recommended screening tests. This includes screening completion with colonoscopy after a clinically significant abnormal non-colonoscopic screening test requiring follow-up."

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This letter outlines the value of CTC with the increase in screening that will save lives and a reduction in the racial/ethnic disparities that limits colon cancer screening adoption. Extracolonic findings are also addressed as they relate to the draft USPSTF recommendation.

**Increased Colorectal Cancer Screening Rates Using CTC**

In 2018, the American Cancer Society published their updated guidelines for colorectal cancer screening, which concluded that adults aged 45 years and older with an average risk of colorectal cancer should undergo regular screening using one of a variety of available screening options, including CTC every 5 years[1].

Literature shows an increase in colorectal cancer screening rates with the introduction of CTC as a covered screening option. In both the University of Wisconsin and Colon Health Initiative (CHI) experiences, colorectal cancer screening adherence improves with the implementation of CTC[2,3,4]. As opposed to substituting one exam for the other, the addition of CTC to the current menu of CRC screening options appears to increase overall rates. At the former National Naval Medical Center (now Walter Reed National Military Medical Center), since 2005, colorectal screening has increased by 33 percent with more than 70 percent of beneficiaries compliant with CRC recommendations following the integration of CTC screening with the existing colonoscopic program. Another study demonstrated improved Healthcare Effectiveness Data and Information Set (HEDIS) compliance, up to 84% for colorectal cancer screening with the inclusion of CTC[5].

On October 2016, the National Committee for Quality Assurance (NCQA) released the Healthcare Effectiveness Data and Information Set (HEDIS) 2017 Technical Specifications Update, which included the addition of CTC to the colorectal cancer screening measure[6].

A study of 250 average-risk patients undergoing colorectal cancer screening found that the most common reasons for choosing CTC included convenience (33.6%), recommendation by a referring provider (13.2%), and safety (10.8%). If CTC were not an available option, 36% of the 250 enrolled patients would not have undergone colorectal cancer screening. Among the 57 patients who underwent both procedures, 95% preferred CTC[7]. In a study of 1,417 adults undergoing CTC screening in three different settings including community practice, academic center, and military medical center the top reason for choosing CTC was an avoidance of the risks and expense of anesthesia. Of 441 respondents who experienced both CTC and colonoscopy, 77.1% preferred CTC, and 13.8% preferred colonoscopy. Of all patients, 19.6%

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[1] Wolf AMD, Fontham ETH, Church TR, et al. Colorectal cancer screening for average-risk adults: 2018 guideline update from the American Cancer Society. *CA Cancer J Clin*. 2018;68:250-281.
[2] Schwartz DC, Dasher KJ, Said A et al. Impact of a CT colonography screening program on endoscopic colonoscopy in clinical practice. Am J Gastroenterol 2008;103:346-351
[3] Cash BD, Riddle M, Bhattacharya I et al, 2008 CT Colonography of a Medicare-Aged Population: Outcomes Observed in an Analysis of More Than 1400 Patients. AJR 2012;199: W27-W34. 10.2214/AJR.11.7729.
[4] Benson M, Pier J, Kraft S et al. Optical colonoscopy and virtual colonoscopy numbers after initiation of a CT colonography program: long term data. J Gastrointest Liver Dis 2012; 21(4):391-395.
[5]Cash BD, Stamps K, McFarland EG, Spiegel AR, Wade SW. Clinical use of CT colonography for colorectal cancer screening in military training facilities and potential impact on HEDIS measures. J Am Coll Radiol 2013;10:30-36.
[6] NCQA Releases 2017 CRC HEDIS Measure. Retrieved from: http://nccrt.org/ncqa-releases-2017-crc-hedis-measure/. Accessed on January 30, 2019.
[7] Moawad FJ, Maydonovitch CL, Cullen PA, et al. CT colonography may improve colorectal cancer screening compliance. AJR 2010;195:1118-1123.

indicated that they may not have undergone colonoscopy screening if CTC were not available. Of all respondents, 93% indicated that they would choose CTC for their next screening[8].

**Implementation**

CTC is easily implemented at sites where there are current model CT scanners. The ACR provides a simple to use CTC locator tool to assist patients and providers find a CT Colonography screening location near them at https://www.acr.org/myctc. CTC is performed without sedation so there is no need for another person to accompany or drive the patient to the imaging center. The patient can resume normal daily activities immediately upon test completion. Additionally, CTC can be performed as a relatively "socially-distanced" examination[9]. Other than during the brief period of rectal tube insertion, greater than 6 feet of separation between patients and healthcare workers can be maintained which is particularly important during a pandemic. Other advantages of CTC include a short procedural time, less direct contact with health care workers given lack of sedation, and extremely low risk of complications requiring in-patient beds. CTC is a structural examination and can triage patients for polypectomy or surveillance depending on lesions found and can better detect precancerous lesions as compared to stool-based tests.

Abnormal findings identified by CTC screening may require additional workup by colonoscopy, though small (6-9 mm) polyps can be followed with surveillance CTC, typically performed at a 3-year interval, as most polyps of this size remain stable (38-50%) or regress (27-28%) with a minority (22-35%) of polyps progressing[10, 11].

Under current ACA requirements, insurance providers required to cover Grade A and B recommendations without cost-sharing will need to cover recommended screening tests. This includes screening completion with colonoscopy after a clinically significant abnormal non-colonoscopic screening test requiring follow-up.

**Stool-Based Tests versus Direct Visualization Tests**

The 2018 ACS guideline update and the current USPSTF draft recommendations divide the CRC screening tests into stool-based screening tests and direct visualization tests. CT colonography is classified as a direct visualization test and is therefore a preventive test allowing identification of the precursor polyp which can then be removed to prevent colorectal carcinoma from ever developing. Stool-based tests are primarily effective for detection of the cancer only rather than the precursor adenomatous polyp.

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[8] Pooler BD, Baumel MJ, Cash BD, et al. Screening CT colonography: multicenter survey of patient experience, preference, and potential impact on adherence. AJR 2012;198:1361-1366. 10.2214/AJR.11.7671

[9] Moreno CC, Yee J, Ahmed FS, et al. CT colonography's role in the COVID-19 pandemic: a safe(r), socially distanced total colon examination. Abdom Radiol 2020. doi: 10.1007/s00261-020-02674-5

[10] Pickhardt PJ, Kim DH, Pooler BD, Hinshaw JL, Barlow D, Jensen D, Reichelderfer M, Cash BD. Assessment of volumetric growth rates of small colorectal polyps with CT colonography: a longitudinal study of natural history. Lancet Oncol 2013;8:711-20. doi: 10.1016/s1470-2045(13)70216-x.

[11] Tutein Nolthenius CJ, Boellaard TN, de Haan MC, et al. Evolution of Screen-Detected Small (6-9 mm) Polyps After a 3-Year Surveillance Interval: Assessment of Growth With CT Colonography Compared With Histopathology. Am J Gastroenterol 2015;110:1682-90.doi: 10.1038/ajg.2015.340

Overall, the accuracy of direct visualization tests such as colonoscopy and CT colonography exceed stool-based tests such as gFOBT, FIT, and sDNA-FIT. While sensitivity for cancer detection is fair to good for all the recommended testing options (ranging from 13-75% for gFOBT and 73.8% for FIT to 92.3% for sDNA-FIT, 89-95% for colonoscopy, and 96.1% for CT colonography), sensitivities for clinically significant polyps vary more widely with sensitivities for high-grade adenomas at only 7-41% for gFOBT, 15-30% for FIT, and 42.4% for sDNA-FIT versus 88.2% for colonoscopy and 90% for CT colonography[12,13,14,15,16,17,18]. As noted in the draft recommendation, the accuracy quoted for CT colonography should be in the higher end of the stated range given that most trials showing better results over the last 17 years have benefited from the use of current standard-of-care techniques which now include routine use of oral contrast for fecal/fluid tagging, multi-detector CT with 3D reconstruction, and experienced readers.

The joint guideline strongly stated that colorectal cancer prevention should be the primary goal of screening emphasizing the central role of direct visualization tests. For this reason, it would be more impactful to list direct visualization tests ahead of stool-based tests in both the text and tables of the updated USPSTF Recommendation.

**Benefits of Early Detection and Treatment**

The USPSTF is well aware of the disturbing increase in the incidence of colorectal cancer amongst those under 50 years of age. Those born in the1990s have double the risk of colon cancer (IRR = 2.40, 95% CI = 1.11 to 5.19) and quadruple the risk of rectal cancer (IRR = 4.32, 95% CI = 2.19 to 8.51) compared to those born in the 1950s.[19-20] With colorectal cancer incidence at 45 years of age now similar to 50 year olds back in the 1990s when USPSTF colorectal cancer screening recommendations were first drafted, the move to recommend screening at age 45 is well justified.[21] The current list of screening options made available at age 45 not only results in significant life-years gained for all options but is also well justified in multiple

[12] Pickhardt PJ et al. Computed tomographic virtual colonoscopy to screen for colorectal neoplasia in asymptomatic adults NEJM 2003;349:2191-2200.
[13] Johnson CD et al. Accuracy of CT colonography for detection of large adenomas and cancers. NEJM 2008;359:1207-1217.
[14] Imperiale TF et al. Multitarget stool DNA testing for colorectal-cancer screening. NEJM 2014;370:1287-1297.
[15] Pickhardt PJ et al. Colorectal cancer: CT colonography and colonoscopy for detection--systematic review and meta-analysis. Radiology 2011;259:393-405.
[16] Shapiro JA et al. A Comparison of Fecal Immunochemical and High-Sensitivity Guaiac Tests for Colorectal Cancer Screening. Am J Gastroenterol 2017;112(11):1728-1735.
[17] Allison JE et al. Screening for colorectal neoplasms with new fecal occult blood tests: update on performance characteristics.J Natl Cancer Inst 2007;99(19):1462-70.
[18] Ahlquist DA et al. Stool DNA and occult blood testing for screen detection of colorectal neoplasia. Ann Intern Med 2008;149(7):441-50, W81.
[19] Siegel RL, Fedewa SA, Anderson WF, et al. Colorectal cancer incidence patterns in the United States, 1974-2013. J Natl Cancer Inst. 2017;109(8):djw322.
[20] Pearlman et al. Prevalence and Spectrum of Germline Cancer Susceptibility Gene Mutations Among Patients With Early-Onset Colorectal Cancer. JAMA Oncol 2017.
[21] Megna B, Shaukat A. Is 45 the new 50? Controversies in lowering the screening age for colorectal cancer, Expert Review of Gastroenterology & Hepatology (2019), 13:10, 915-917, doi:10.1080/17474124.2019.1681973

cost-effectiveness analyses[22,23,24]. This is particularly true given the larger economic consequences of colorectal cancer when affecting those in their prime working years. As a screening option for the under 50 age group, CT colonography is particularly attractive in not requiring anesthesia or transportation to or from the screening examination. This results in significantly less economic impact from the test itself while preserving the preventive advantages of a direct visualization test, especially for a group with significantly more potential productive life-years to save.

Screening rates in patients in their early 50s still remain relatively low due to a lag in screening uptake (only 58% in those 50-54 years old compared to 68% in those 55-64)[25]. Lowering the screening age to 45 may also aid in boosting rates in those older than 50 resulting in additional productive life-years saved. Similarly, lowering the overall screening age for average-risk individuals may improve screening rates in Black adults, a higher risk group who should already be starting screening at the age of 45 under pre-existing guidelines.

**Reduced Racial/Ethnic Disparities in Screening**

CTC has been found to be a preferred screening test option in vulnerable patients. A study evaluating preferences for colorectal cancer screening among racially and ethnically diverse patients found that ratings of CTC were significantly higher than ratings of colonoscopy, sigmoidoscopy, and fecal occult blood testing in Black and Latinx patients[26].

A study evaluating the performance of CTC in a screening cohort of 2490 Black adults found that CTC was an effective screening modality with a per-patient CTC positive rate of 9.8% for polyps measuring 6 to 9 mm, 5.4% for polyps measuring 10 to 29 mm, and 1.3% for masses ≥ 30 mm. The referral rate to optical colonoscopy was 13.9%[27].

While USPSTF is tasked with providing guidelines that guide the average-risk population, the guidelines do not adequately address the incidence and mortality variability based on race/ethnicity and gender differences. It is suggested USPSTF further examine variance in incidence, mortality, and screening rates for the: Black American Population, Latinx, and Indigenous Populations to make specific considerations for subpopulations.

[22] Gastroenterology. Cost-Effectiveness and National Effects of Initiating Colorectal Cancer Screening for Average-Risk Persons at Age 45 Years Instead of 50 Years. 2019 Jul;157(1):137-148. doi: 10.1053/j.gastro.2019.03.023. Epub 2019 Mar 28.
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[24] BMC Gastroenterol. Effectiveness, benefit harm and cost effectiveness of colorectal cancer screening in Austria.2019 Dec 5;19(1):209. doi: 10.1186/s12876-019-1121-y.
[25] Siegel RL, Miller KD, Sauer AG, et al. Colorectal cancer statistics, 2020. CA: A Cancer Journal for Clinicians. https://acsjournals.onlinelibrary.wiley.com/doi/full/10.3322/caac.21601
[26] Hawley ST, Volk RJ, Krishnamurthy P, et al. Preferences for colorectal cancer screening among racially/ethnically diverse primary care patients. Med Care 2008;46:S10-6.
[27] Moreno CC, Fibus TF, Krupinski EA, Kim DH, Pickhardt PJ. Addressing racial disparity in colorectal cancer screening with CT colonography: experience in an African-American cohort. Clin Colorectal Cancer 2018;17(2):e363-e367.

**Extracolonic findings at CTC**

Extracolonic findings (ECF) have led to debate and misunderstanding in terms of their incidence and impact in screening cohorts at CTC. Although relatively higher rates have been reported in symptomatic patients, including patients with colon cancer and metastatic disease[28,29,30], low rates of clinically significant ECF of 4.5 to 16% have been reported in large screening cohorts[31]. Equally as important is the actual rate of additional imaging or work-up which occurs, which demonstrates the true impact of these findings.

A large meta-analysis of ECF in CTC was published in 2018 including 44 studies of both screening and symptomatic cohorts (49,676 patients) from 1994 to 2017[32]. The pooled rate of potentially important findings was 4.9% (95% CI 3.7-6.4%). Importantly with longer-term follow-up of extracolonic findings, this estimate declined over time, averaging 9% decrease per year since 2006, and was significantly lower with the use of the C-RADS reporting system for CTC. The overall pooled rates of recommended workup were 4.0% for potentially important ECF.

A screening cohort of 2,490 Black adults (85% male) reported a rate of 4% for E4 (potentially important) findings in patients 50 to 80 years old[33]. Another series of over 3,000 low risk but symptomatic patients was published in 2017, with a rate of 2.0% for E4 ECF findings[34]. These large series continue to demonstrate the low rates of clinically significant ECF at CTC.

A study comparing ECF rates in screening and diagnostic CTC patient cohorts found low rates in both. 4.6% of patients with E3/E4 findings in the screening cohort demonstrated clinically significant outcomes, compared with 4.0% in the diagnostic cohort, including a total of three extracolonic malignancies (0.8%) and three abdominal aortic aneurysms (0.8%)[35]. The distribution of extracolonic findings and clinical outcomes were not statistically significantly different between screening and diagnostic CTC populations.

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[28] Kahn KY, Xiong T, McCafferty I et al. Frequency and impact of extracolonic findings detected at computed tomography in a symptomatic population. British J of Surgery 2007;94:355-361.

[29] Flicker MS, Tsoukas AT, Hazra A. Economic impact of extra-colonic findings at computed tomographic colonography. J Comput Assist Tomogr 2008;32:497-503.

[30] Hellstrom M, Svensson MH, and Lasson A. Extracolonic and incidental findings on CT colonography (virtual colonoscopy). AJR 2004; 182:631-638.

[31] 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.

[32] Pickhardt PJ, Correlate L, Morra L, Regge D, Hassan C. Extra-colonic findings at CT colonography: systematic review and meta-analysis. AJR 2018;211:25-39.

[33] Moreno CC, Fibus TF, Krupinski EA, Kim DH, Pickhardt PJ. Addressing racial disparity in colorectal cancer screening with CT colonography: experience in an African-American Cohort. Clin Colorectal Cancer. 2018 Jun;17(2):e363-e367. doi: 10.1016/j.clcc.2018.02.007. Epub 2018 Feb 20.

[34] Netz FRS, Pickardt PJ, Heijnen MLG, Simons PCD. Detections of potentially relevant extra-colonic findings at CT colonography in a low risk symptomatic patient population. Abdom Radiol 2017;42:2799-2806).

[35] Taya M, McHargue C, Ricci ZJ, Flusberg M, Weinstein S, Yee J. Comparison of extracolonic findings and clinical outcomes in a screening and diagnostic CT colonography population. Abdom Radiol. 2018 Sep 12. doi: 10.1007/s00261-018-1753-3. [Epub ahead of print]

In addition to the use of the C-RADS reporting structure for quality assurance, significant efforts by the ACR Incidental Findings Committee has led to numerous guidelines regarding standardization and optimizing the reporting of incidental findings in radiology[36,37,38,39,40].

One issue not often addressed, but which must be included in discussions on the efficacy of CTC is the benefits of extracolonic diagnoses. There are serious findings that could be discovered to the patient's benefit, including extracolonic (EC) cancers and abdominal aortic aneurysms (AAA). Veerappan et al. reported that the prevalence of EC cancers was equivalent to unsuspected colorectal cancers in their large screening series (n=2,277)[41]. Similar results were seen in a larger screening cohort of over 10,000 patients where the extracolonic cancer prevalence was 0.35% whereas the colorectal cancer prevalence was 0.21%[42]. The AAA prevalence has been reported at 0.5% (up to 1% in screening males)[43]. The benefits of screening for AAA have already been established for older males—and these can be accurately detected at CTC due to its cross-sectional nature. Hassan et al. modeled the impact of incorporating the impact of extracolonic neoplasms and AAA into CTC screening[44]. This group demonstrated that there were substantial gains in life years by CTC screening because of the coincident ability of CTC to detect AAA in addition to detecting colorectal high-risk lesions.

[36] Berland LL, Silverman SG, Gore RM, et al. Managing incidental findings on abdominal CT: white paper of the ACR incidental findings committee. J Am Coll Radiol 2010; 7:754-773.
[37] Patel MD, Ascher SM, Paspulati RM, et al. Managing Incidental Findings on Abdominal and Pelvic CT and MRI, Part 1: White Paper of the ACR Incidental Findings Committee II on Adnexal Findings. J Am Coll Radiol 2013;10:675-681.
[38] Heller MT, Harisinghani M, Neitlich JD, Yeghiayan P, Berland LL. Managing Incidental Findings on Abdominal and Pelvic CT and MRI, Part 3: White Paper of the ACR Incidental Findings Committee II on Splenic and Nodal Findings. J Am Coll Radiol 2013;10-833-839.
[39] Sebastian S, Araujo C, Neitlich JD, Berland LL. Managing Incidental Findings on Abdominal and Pelvic CT and MRI, Part 4: White Paper of the ACR Incidental Findings Committee II on Gallbladder and Biliary Findings. J Am Coll Radiol 2013;10:953-956.
[40] Doshi AM, Kiritsy M, Rosenkrantz AB. Strategies for avoiding recommendations for additional imaging through a comprehensive comparison with prior studies. J Am Coll Radiol 2015;12:657-663.
[41] Veerappan GR, Ally MR, Choi JR, et al. Extracolonic findings on CT colonography increases yield of colorectal cancer screening. AJR. 2010;195:677-686.
[42] Pickhardt PJ, Hanson ME. Incidental adnexal masses detected at low-dose noncontrast CT in asymptomatic women over 50 years of age: implications for clinical management and ovarian cancer screening. Radiology 2010; 257:144–150.
[43] Pickhardt PJ, Hanson ME, Vanness DJ, et al. Unsuspected extracolonic findings at screening CT colonography: clinical and economic impact. Radiology. 2008;249:151-159.
[44] Hassan C, Pickhardt PJ, Laghi A, et al. Computed tomographic colonography to screen for colorectal cancer, extracolonic cancer, and aortic aneurysm: model simulation with cost-effectiveness analysis. Arch Intern Med. 2008;168:696-705.

**Summary**

In summary, the ACR strongly supports the proposed USPSTF recommendation of a Grade A for colorectal cancer screening in adults ages 50 to 75 years and a Grade B for colorectal cancer screening in adults ages 45 to 49 years. The cited peer-reviewed literature provides continued and new evidence confirming the efficacy and safety of CTC and fully supports the inclusion of CTC as a validated option for colorectal cancer screening.

Additionally, we support clarification of the importance of completing screening with colonoscopy after a clinically significant abnormal non-colonoscopic screening test (such as after a CTC) which will allow the U.S. population to achieve the full benefits of their colorectal cancer screening recommendations.

We appreciate the opportunity to provide these comments. Should you have any questions or comments, we would welcome further dialogue. Please do not hesitate to contact Kathryn Keysor at (800) 227-5463 extension 4950 or at kkeysor@acr.org.

Sincerely,

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