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By Online Submission

Re: National Coverage Reconsideration for Screening Computed Tomography Colonography (CTC) for Colorectal Cancer (CAG-00396N)

Dear Ms. Syrek Jensen,

The Colon Cancer Alliance (CCA), Colon Cancer Coalition (CCC), Prevent Cancer Foundation (PCF), Society of Abdominal Radiology (SAR), Society of Computed Body Tomography & Magnetic Resonance (SCBT-MR), American College of Radiology (ACR)[1], Medical Imaging Technology Alliance (MITA), BRACCO, and iCAD, a Coalition representing colorectal cancer patients, diagnostic radiologists, radiation oncologists, nuclear medicine physicians, medical physicists, body and abdominal imagers, and manufacturers, formally request the opening of national coverage reconsideration for screening Computed Tomography Colonography (CTC) for colorectal cancer (CAG-00396N). The CCA, CCC, PCF, SAR, SCBT-MR, ACR, MITA, BRACCO, and iCAD, hereafter referred to as the "CTC Coalition," agree with the recent United States Preventive Services Task Force (USPSTF) final recommendation of grade "A" for colorectal cancer screening in those age 50-75 years with a list of recognized screening exams including CTC.

The CTC Coalition requests that the Centers for Medicare and Medicaid Services (CMS) implement the United States Preventive Services Task Force (USPSTF) recommended CTC CRC screening test and extend this life saving benefit to the Medicare population under the National Coverage Determination/Reconsideration process. We agree with the USPSTF that strong evidence demonstrates that screening for colorectal cancer (CRC) with various proven options, including CTC, can accurately detect precursor adenomatous polyps and early stage colorectal cancer, and that screening for CRC in adults age 50 and older including Medicare-age individuals reduces mortality due to this malignancy.

[1] ACR is a professional organization representing more than 35,000 radiologists, radiation oncologists, interventional radiologists, nuclear medicine physicians, and medical physicists.

Background

Colorectal cancer is the second most commonly diagnosed cancer in the United States and the overall second leading cause of cancer deaths even though it has a 90% cure rate with early detection.

Over 140,000 Americans are diagnosed with CRC every year, and nearly 50,000 men and women die due to late detection[2]. Less than half of adults 50 years of age and older are compliant with recommended screening in the United States[3] with the existing CMS covered screening options.

CTC is endorsed by the American Cancer Society, the U.S. Multi-Society Task Force, the ACR, the Food and Drug Administration, and the USPSTF as a recommended test for CRC screening. A positive coverage determination by CMS will result in broader dissemination and education of CTC to the public and will also help close the gap in CRC screening rates between whites and minority populations[3,4]. The USPSTF final recommendation highlights that colorectal cancer is most frequently diagnosed among adults age 65 to 74. As such, providing Medicare patients with access to CTC will promote early detection and will save many thousands of lives. It is now time for CT colonography to be recognized by Medicare as an approved screening test[5].

The CTC Coalition agrees that the overarching public health priority is to ensure equitable access to high quality screening programs built on existing frameworks of evidence-based protocols and multi-disciplinary care according to best practices. The USPSTF highlights that there are "no empirical data to suggest that any of the screening strategies provide a greater net benefit." However, the USPSTF determined that CISNET modeling suggests that screening every 5 years with CT colonography (assuming colonoscopy follow-up for lesions measuring ≥6 mm) from ages 50-75 years potentially yields approximately the same number of life-years gained, with a similar balance of benefits and harms, as other recommended strategies including FIT, FOBT, flexible sigmoidoscopy + FIT, and colonoscopy).

Additionally, the USPSTF states that clinicians should engage patients in informed decision making about the screening strategy that would most likely result in completion, with high adherence over time, taking into consideration both the patient's preferences and local availability. They further note that screening for colorectal cancer is "substantially underused" and that "the best screening test is the one that gets done"[6].

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[2] Siegel R, Naishadham D, Jemal A. Cancer statistics, 2012. CA Cancer J Clin 2012; 62:10–29.

[3] American Cancer Society. Colorectal cancer facts & figures 2011–2013. Atlanta, GA: American Cancer Society, 2011.

[4] Moawad FJ, Maydonovitch CL, Cullen PA, et al. CT colonography may improve colorectal cancer screening compliance. AJR 2010; 195:1118–1123.

[5] Yee J, Keysor KJ, Kim DH. The time has arrived for national reimbursement of screening CT colonography. AJR 2013; 201.

[6] US Preventive Services Task Force. Screening for Colorectal Cancer: US Preventive Services Task Force Recommendation Statement. JAMA. 2016;315(23):2564-2575.

In 2009, CMS determined that there was inadequate evidence to support national coverage of CTC as a colorectal cancer screening test echoing the 2008 USPSTF rating of "I" (insufficient evidence) rating for CTC for colorectal cancer screening. Since that time, additional evidence has documented the value of CTC for colorectal cancer screening and has led to a reversal of the USPSTF prior position.

In the updated evidence report and systematic review for the USPSTF by Lin et al., it was found that four (n= 4,821) of nine CTC studies allowed for estimation of sensitivity of colonoscopy generalizable to community practice. Compared with CTC or colonoscopy plus CTC, it was determined that the sensitivity for colonoscopy to detect adenomas 10 mm and larger ranged from 89-98% and for adenomas 6mm and larger ranged from 75-93%. It was concluded that CTC had sensitivity to detect adenomas 6 mm and larger comparable with colonoscopy. A wider variability in CTC performance was thought possibly due to differences in study design, patient populations studied, bowel preparation, CTC technologies or differences in reader experience. Given the current USPSTF decision to reverse their prior 2008 position on CT colonography and include CTC among the screening tests for screening individuals between 50-75 years of age (based on the interval and existing evidence as well as modeling exercises), the evidence is more than sufficient to allow coverage under the National Coverage Determination/Reconsideration process. As a summary, we present some of the more pertinent evidence which adequately meets and/or exceeds the following two most pertinent questions regarding CTC:

> ***Is the evidence sufficient to determine that CTC is a suitable colorectal cancer screening test for prevention of early detection in Medicare beneficiaries?***
>
> ***Is the evidence sufficient to determine that colorectal cancer screening using CTC is appropriate for Medicare beneficiaries?***

Benefit Category

CRC screening tests have a benefit category under §1832, §1861(s)(2)(R) and §1861(pp) of the Social Security Act. Specifically, the national coverage determination authority under section 1861(pp)(1)(D) (and implementing regulations at 42 CFR 410.37(a)(1)(v)) to determine whether the scope of the CRC screening benefit should be expanded to include coverage of CTC. In addition, since January 1, 2009, CMS is authorized to cover "additional preventive services" if certain statutory requirements are met as provided under §1861(ddd) of the Social Security Act.

Performance in Senior Patient Cohorts

In 2008, the National CTC Trial supported by the National Cancer Institute and administered by the ACR Imaging Network (ACRIN) was published. This landmark study evaluated the accuracy of CTC in a large screening population. Fifteen medical centers participated including both private practice and academic centers. The trial recruited 2,600 asymptomatic individuals. For adenomas 10 mm or larger the per-patient estimates for sensitivity and specificity were 90% and 86%, respectively. Per-patient sensitivity estimates in detecting adenomas ≥ 6 mm, was 78% and per-polyp sensitivity for large neoplasia was 84%.[7] The finding that CTC screening identified 90% of asymptomatic patients with neoplasia ≥ 10 mm correlated with and augmented other published data supporting the role of CTC in average-risk CRC screening.[8]

In another large study the diagnostic yields of CTC and colonoscopy for advanced neoplasia were compared in parallel screening programs[9]. Primary CTC screening in 3,120 patients was compared with primary colonoscopy screening in 3,163 subjects. Similar detection rates were found for CTC and colonoscopy screening, which identified 123 and 121 advanced neoplasms, respectively. The referral rate for colonoscopy in the CTC group was 8%. The total numbers of polyps removed in the CTC and colonoscopy groups were 561 and 2,434, respectively. Seven perforations occurred in the colonoscopy group, but there were none in the CTC group. A review of a 1-year CTC screening experience for colorectal neoplasia showed that 3.9% of individuals had 1 polyp ≥1 cm, and 6.9% had ≥1 polyps 6–9 mm. Of the 71 patients who chose colonoscopy for further evaluation of these polyps, concordant lesions were found with colonoscopy in 65 (91.5% positive predictive value)[10]. In addition, the outcomes of patients with negative CTC screens have also been reported. A longitudinal follow-up of 1,011 patients over nearly 5 years demonstrated a single-interval cancer (crude cancer incidence of 0.2 cancers per 1,000 patient years), leading to the conclusion that a 5-year routine screen interval and non-reporting of diminutive lesions (≤ 5 mm) were appropriate strategies[11].

In the 2009 non-coverage determination, CMS pointed to the need for documentation of the generalizability of the evidence for CTC performance to the Medicare population. Subsequent studies have shown that CTC performance does indeed translate to an older Medicare population.

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[7] Johnson CD, Chen MH, Toledano AY, et al. The National CT Colonography Trial: Multicenter Assessment of Accuracy for Detection of Large Adenomas and Cancers. N Engl J Med 2008; 359:1207-1217.

[8] Pickhardt PJ,Choi JR, Hwng I, et al. Computed tomographic virtual colonoscopy to screen for colorectal neoplasia in asymptomatic adults. N Engl J Med 2003; 349:2191-2200.

[9] Kim DH, Pickhardt PJ, Taylor AJ, et al. CT colonography versus colonoscopy for the detection of advanced neoplasia. N Engl J Med. 2007;357(14):1403-1412.

[10] Pickhardt PJ, Taylor AJ, Kim DH, Reichelderfer M, Gopal DV, Pfau PR. Screening for colorectal neoplasia with CT colonography: initial experience from the 1st year of coverage by third-party payers. Radiology.2006;241(2):417-425.

[11] Kim DH, Pooler BD, Weiss JM, Pickhardt PJ. Five year colorectal cancer outcomes in a large negative CT colonography screening cohort. Eur Radiol. 2012;22(7):1488-1494.

A post hoc analysis of 477 senior patients from the ACRIN National CT Colonography Trial was performed by Johnson et al.[12]; their results showed that the sensitivity and specificity for large neoplasms among the older cohort were 82% and 83%, respectively. There was no statistically significant difference compared with the sensitivity and specificity of 92% and 86%, respectively, for lesions 10 mm or larger in the younger patient cohort. For lesions 6 mm or larger, the respective sensitivity and specificity were 72% and 86% for older patients and 81% and 89% for younger patients, again with no statistically significant difference.

In a retrospective analysis of 577 subjects ranging between 65 and 79 years old (mean age, 69.2 years), Kim et al. found an excellent CTC-OC (Optical Colonoscopy) concordance rate of 91%, indicating that CTC findings can match OC findings in the Medicare population[13]. There was no statistically significant difference in the major characteristics of advanced neoplasms including size, histology, morphology, and location when comparing the older cohort with the general screening cohort. The prevalence of advanced neoplasia was 7.6% for the older age group, which is more than double that found in the general screening population. This result strongly suggests that at a minimum, relative CTC performance is maintained in an older cohort. When a 6-mm threshold was used, there was an overall senior patient referral rate of 15% for colonoscopy. When only adenomas were considered, the per-patient positivity rates for 6-mm and 10-mm thresholds were 11% and 7%, respectively.

Another large series of older military personnel demonstrated similar findings. Cash et al. reported on a sub-analysis of the Colon Health Initiative (CHI) at the National Naval Medical Center in Bethesda MD for patients 65 years of age or older. Ultimately, the results of 1,410 consecutive patients in this age group were reported. Like the above mentioned studies, the Naval series showed similar rates with a colonoscopy referral rate of 14.5% from a positive CTC.[14] Colorectal neoplasia was found in 9.3% of patients.

And finally, a series from New York University (n=454) showed a similar polyp prevalence between the senior (65 years and older) and nonsenior cohort (13.2 versus 14.2; p=0.8). The advanced adenoma prevalence was not reported.[15]

Thus, from the interval body of studies, it is evident that the CTC results generalize to the Medicare population. This is not surprising as there is no likely theoretic reason why CTC would

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[12] Johnson CD, Herman BA, Chen MH, et al. The National CT Colonography Trial: assessment of accuracy in participants 65 years of age and older. Radiology 2012;263:401-408.

[13] Kim DH, Pickhardt PJ, Hanson ME, Hinshaw JL. CT colonography: performance and program outcome measures in an older screening population. Radiology 2010;254:493-500.

[14] Cash BD, Riddle M, et al. Observed outcomes with computerized tomographic colonography in a Medicare-aged screening population: an analysis of over 1,400 patients. AJR 2012 199;W27-34.

[15] Macari M, Nevsky G, Bonavita J, et al. CT colonography in senior versus nonsenior patients: extracolonic findings, recommendations for additional imaging, and polyp prevalence. Radiology. 2011 Jun;259(3):767-774. Epub 2011 Apr 5.

underperform in this cohort. As previously stated, the USPSTF has come to a similar decision with the 'A' rating of CRC screening for individuals aged *50-75 years of age* and inclusion of CTC as a recommended screening test, based on their systematic review of the literature and CISNET microsimulations. If the USPSTF felt that there was not value for older Medicare patients, then it stands to reason that the screening ranges would not extend out to 75 years of age.

Extracolonic Findings

In terms of evidence gaps for CTC, the CMS non-coverage determination (2009) pointed out a paucity of data and outcomes studies for incidental extracolonic findings. Their final conclusion was that the balance between cost/harms and benefit was unknown. Since the CMS decision, additional published data has strengthened what is known about this issue. A large body of evidence now exists in the literature, reflecting over a decade of clinical experience. The recent, updated systematic review for the USPSTF (2015) by Lin et al.[16] identified 21 studies (n=38,293) reporting on extracolonic findings identified at CTC in asymptomatic cohorts, including 16 studies in screening populations. Ten studies have been published since the last CMS review. The systematic review noted that although extracolonic findings were frequent (ranging from 27-69%), actual workup rates for incidental extracolonic findings were low in a range of 1.4-11%. These rates confirm prior studies where the workup rates were around 6%[17]. Large screening studies that have calculated the mean per-patient cost associated with extracolonic findings have consistently found that this expense is between $24 and $34 per patient[18-22]. Even when assuming a much larger cost per patient for extracolonic findings, a recent cost analysis found that CTC screening was still less expensive than colonoscopy screening for Medicare beneficiaries[23].

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[16] Lin JS, Piper M, Perdue LA, Rutter C, Webber EM, O'Connor E, et al. Screening for Colorectal Cancer: An Updated Systematic Review for the U.S. Preventive Services Task Force. Evidence Synthesis No. 135. AHRQ Publication No. 14-05203-EF-1. Rockville, MD: Agency for Healthcare Research and Quality; 2015.

[17] Pickhardt PJ, Hanson ME, Vanness DJ, et al. Unsuspected extracolonic findings at screening CT colonography: clinical and economic impact. Radiology 2008;249:151-9.

[18] Pickhardt PJ, Hanson ME, Vanness DJ, et al. 249:151-9.

[19] Chin M, Mendelson R, Edwards J, Foster N, Forbes G. Computed tomographic colonography: Prevalence, nature, and clinical significance of extracolonic findings in a community screening program. American Journal of Gastroenterology 2005;100:2771-6.

[20] Gluecker TM, Johnson CD, Wilson LA, et al. Extracolonic findings at CT colonography: Evaluation of prevalence and cost in a screening population. Gastroenterology 2003;124:911-6.

[21] Hara AK, Johnson CD, MacCarty RL, Welch TJ. Incidental extracolonic findings at CT colonography. Radiology 2000;215:353-7.

[22] Yee J, Kumar NN, Godara S, et al. Extracolonic abnormalities discovered incidentally at CT colonography in a male population. Radiology 2005;236:519-26.

[23] Pyenson B, Pickhardt PJ, Sawhney TG, Berrios M. Medicare cost of colorectal cancer screening: CT colonography vs. optical colonoscopy. Abdom Imaging 2015 Sep 9. [Epub ahead of print].

On the benefit side, a recently published large, long term study of significant extracolonic findings at CTC screening clearly addresses an evidence gap, reporting longer term outcomes data[24]. Pooler et al. reported on outcomes from a cohort of nearly 8,000 consecutive individuals screened over an 8-year period. Overall, potentially important extracolonic findings (C-RADS E4) were identified in 2.5% (202 of 7,952 adults), the majority of which ultimately proved to be relevant, including unsuspected extracolonic tumors in 42 individuals and abdominal aneurysms in 57 individuals. In the minority of patients with findings that proved to be benign or otherwise clinically insignificant, there were no significant complications related to their work-up. This new information allows for a better understanding of the net benefit associated with this screening approach. It reinforces what has been seen in modeling studies where the addition of extracolonic findings can add to life year gained while showing cost benefits.[25,26] It is thus clear that the interval literature has helped to define the balance between the costs and harms of incidental extracolonic workup against the potential benefits of diagnosing serious but unknown conditions.

The issue of incidental findings is not unique to CTC but exists for many other diagnostic tests, including all cross-sectional radiologic imaging. As such, radiologists are familiar with the responsible handling of unsuspected findings, including when additional evaluation is indicated. Radiologists understand the importance to distinguish insignificant/unimportant findings that require no additional studies for those that are potentially significant and may require further evaluation and possibly intervention. In order to maximize the benefit to the patient and mitigate against unnecessary expense and morbidity, the Virtual Colonoscopy Working Group proposed a C-RADS categorization of extracolonic findings in 2005[27], which has been adopted widely among practices performing CTC. In addition, the ACR quality metrics in the CTC National Radiology Data Registry (NRDR) includes reporting of extracolonic findings that require additional work-up, which will allow for continued monitoring of outcomes.

Separate from C-RADS, the ACR Incidental findings committee published a comprehensive White Paper manuscript in 2010 regarding the management of incidental findings at abdominal CT[28]. This manuscript outlines important algorithms of how to follow or ignore common incidental findings based on size and morphology in both the general population and patients with limited life

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[24] Pooler BD, Kim DH, Pickhardt PJ. Potentially important extracolonic findings at screening CT colonography: incidence and outcomes data from a clinical screening program. AJR 2015 Oct 22:1-6. [Epub ahead of print].

[25] 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 Apr 14;168(7):696-705.

[26] Pickhardt PJ, Hassan C, Laghi A, Kim DH. CT colonography to screen for colorectal cancer and aortic aneurysm in the medicare population: cost effectiveness analysis. AJR 2009;192:1332-1340.

[27] Zalis ME, Barish MA, Choi JR, et al. CT colonography reporting and data system: a consensus proposal. Radiology 2005; 236:3–9.

[28] 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.

expectancy and/or co-morbidity. This provides useful guidelines on how to manage common findings at CTC, such as hypodense liver and renal lesions, so as to decrease unnecessary follow up. Since its publication, these algorithms have been further promoted throughout major radiology organizations including the Society of Abdominal Radiology (SAR), Society of Computed Body Tomography and Magnetic Resonance (SCBT/MR), and the Radiological Society of North America (RSNA).

Radiation Dose

In the prior non-coverage determination, CMS includes radiation-induced cancer as a potential long term concern with repeated use of CT colonography and states there are no studies that directly measured this risk.

Prior reports have discussed the controversy of low radiation dose exposure[29-31]. Since then there have been significant advances made in the reduction of radiation dose amongst all types of CT examinations. Much of this has been through the widespread use of reconstructions techniques such as iterative reconstruction as well as through the use of decreased tube voltage and automatic dose modulation[32,33]. As a result, much of the radiation dose data referenced by the AHRQ report from Lin et. al. from between 2003-2013 is already outdated. There have been more substantial dose reductions in CTC recently with all publications related to radiation dose and CTC within the past 2 years now showing average doses ranging from less than 1 mSv up to 2 mSv [34- 43]. This was

[29] Amis ES, Jr., Butler PF, Applegate KE, et al. American College of Radiology white paper on radiation dose in medicine.J Am Coll Radiol. 2007;4(5):272-284.

[30] Brenner DJ, Hall EJ. Computed tomography--an increasing source of radiation exposure. N Engl J Med. 2007;357(22):2277-2284.

[31] Smith-Bindman R, Miglioretti DL, Johnson E, et al. Use of diagnostic imaging studies and associated radiation exposure for patients enrolled in large integrated health care systems, 1996-2010. JAMA. 2012;307(22):2400-2409.

[32] Chang KJ, Yee J. Dose reduction methods for CT colonography. Abdom Imaging. 2013;38(2):224-232.

[33] McCollough CH, Chen GH, Kalender W, et al. Achieving routine submillisievert CT scanning: report from the summit on management of radiation dose in CT. Radiology. 2012;264(2):567-580.

[34] Chang KJ, Heisler MA, Mahesh M, Baird GL, Mayo-Smith WW. CT colonography at low tube potential: using iterative reconstruction to decrease noise. Clin Radiol. 2015;70(9):981-988.

[35] Lambert L, Danes J, Jahoda J, Masek M, Lisy J, Ourednicek P. Submilisievert ultralow-dose CT colonography using iterative reconstruction technique: a feasibility study. Acta Radiol. 2015; 56(5):517-525.

[36] Lambert L, Ourednicek P, Jahoda J, Lambertova A, Danes J. Model-based vs hybrid iterative reconstruction technique in ultralow-dose submillisievert CT colonography.Br J Radiol. 2015; Apr;88 (1048) :20140667.

[37] Lubner MG, Pickhardt PJ, Kim DH, Tang J, del Rio AM, Chen GH. Prospective evaluation of prior image constrained compressed sensing (PICCS) algorithm in abdominal CT: a comparison of reduced dose with standard dose imaging. Abdom Imaging.

[38] Lubner MG, Pooler BD, Kitchin DR, et al. Sub-milliSievert (sub-mSv) CT colonography: a prospective comparison of image quality and polyp conspicuity at reduced-dose versus standard-dose imaging. Eur Radiol. 2015;25(7):2089-2102.

also noted in the Lin et al. report who found that recent CTC screening studies showed lower radiation doses. Comparison of the radiation exposure of CTC to radiation exposures from naturally occurring sources is helpful in placing the very low dose of radiation from CTC into proper context. Current doses are lower than the annual background radiation exposure from natural sources of 3 mSv/year (U.S. range 1-10 mSv/year).

While high doses of whole body radiation (on the order of Hiroshima and Nagasaki atomic bomb survivors) have been associated with increased cancer risks, at the very low doses used in medical imaging, the "risks of health effects are either too small to be observed or are nonexistent"[44]. Low doses of radiation are defined as those below 100 mSv. Thus, CTC is an extremely low dose procedure, even when tabulating estimated total exposure in a program of CT Colonography-based screening. The National Academies of Sciences (2006), the Health Physics Society (2010), and the American Association of Physicists in Medicine (2011) all discourage the calculation of risk below 50-100 mSv, because it is too small to estimate with any accuracy given the available data[44,45]. Theoretical rates of cancer induction also drop significantly after the age of 35, a critically important factor to consider when the colorectal screening population is age 50 or older[46]. In addition, any theoretical risks using whole body exposure are overestimated based on the finite anatomic coverage of CTC of only the abdomen and pelvis being exposed.

Based on the older dose data, multiple benefit-risk analyses have been performed assessing the benefits of colorectal screening using CT colonography against the theoretical risks related to low dose radiation exposure in the screening population[47,48]. The estimated potential lifetime cancer

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[39] Millerd PJ, Paden RG, Lund JT, et al. Reducing the radiation dose for computed tomography colonography using model-based iterative reconstruction. Abdom Imaging. 2015;40 (5):1183-1189.

[40] Nagata K, Fujiwara M, Kanazawa H, et al. Evaluation of dose reduction and image quality in CT colonography: comparison of low-dose CT with iterative reconstruction and routine-dose CT with filtered back projection. Eur Radiol. 2015;25(1):221-229.

[41] Shen H, Liang D, Luo M, et al. Pilot study on image quality and radiation dose of CT colonography with adaptive iterative dose reduction three-dimensional. PloS one. 2015;10(1):e0117116.

[42] Shin CI, Kim SH, Lee ES, et al. Ultra-low peak voltage CT colonography: effect of iterative reconstruction algorithms on performance of radiologists who use anthropomorphic colonic phantoms. Radiology. 2014;273(3):759-771.

[43] Yamamura S, Oda S, Imuta M, et al. Reducing the Radiation Dose for CT Colonography: Effect of Low Tube Voltage and Iterative Reconstruction. Acad Radiol. 2015 Apr 11. pii: S1076-6332(15)00130-0. doi: 10.1016/j.acra.2015.03.009. [Epub ahead of print].

[44] Burk RJ. Radiation risk in perspective: position statement of the Health Physics Society. hpsorg/documents/risk_ps010-2pdf. Revised 2010. Accessed October 22, 2015.

[45] American Association of Physicists in Medicine. AAPM Position Statement on Radiation Risks from Medical Imaging Procedures. http://www.aapm.org/org/policies/details.asp?id=318&type=PP&current=true. Accessed October 22, 2015.

[46] Burk RJ.October 22, 2015.

[47] Berrington de Gonzalez A, Kim KP, Knudsen AB, et al. Radiation-related cancer risks from CT colonography screening: a risk-benefit analysis. AJR Am J Roentgenol. 2011;196(4):816-823.

risk was calculated to be extremely low in the range of 0.06%-0.14% for a single CTC exam at the age of 50. When compared to the overall lifetime risk of cancer of 40%[49], the risk of CTC is insignificant. These analyses have shown that the benefits of CTC for screening vastly outweigh the risks by an order of 24:1 to 35:1, even when accounting for any additional risks from the imaging workup of incidental extracolonic findings. Thus, even if the highly controversial risk models (such as the linear non-threshold model) used in these studies were accurate, the authors conclude that the net benefit to risk ratio is very high and could potentially be even higher (by a factor of 5 or 10) when using current low dose protocols.

The published data show that the estimated potential lifetime risk of radiation induced cancers is extremely low and the benefit of colorectal cancer screening with CTC vastly outweighs any theoretical risk. Low radiation dose lung cancer screening recently became a covered test by Medicare and so should CTC.

CTC Training and Experience

CTC interpretation training and experience guidelines were established for radiologists by the American College of Radiology (ACR)[50], for non-radiologists by the American Gastroenterological Association (AGA)[51,52] and by an International collaborative group[53].

Several Continuing Medical Education (CME) approved educational opportunities were developed and offered over the last decade by industry, academic institutions (e.g. University of Wisconsin) and society sponsored national meetings (e.g., Society of Abdominal Radiology). To accommodate the demand for training, the ACR Education Center developed a CTC training course in 2007, accredited by the Accreditation Council for Continuing Medical Education, which meets or exceeds the ACR guidelines providing both lectures (covering patient preparation, scanning parameters and recognition of pitfalls) and hands-on software training and evaluation of at least 50 highly selected colonoscopy-proven cases in a controlled environment accommodating up to 60 students interacting with faculty (radiologists and software experts). All cases are evaluated in a testing mode and trainees are required to correctly diagnose abnormalities and recognize pitfalls.

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[48] Brenner DJ, Georgsson MA. Mass screening with CT colonography: should the radiation exposure be of concern? Gastroenterology. 2005;129(1):328-337.

[49] SEER Cancer Statistics Review 1975-2012. http://seer.cancer.gov/csr/1975_2012/. Accessed October 22, 2015.

[50] McFarland EG, Fletcher JG , Pickhardt P ,et al . ACR Colon Cancer Committee white paper: status of CT colonography 2009 .J Am Coll Radiol 2009; 6 (11): 756-772.e4.

[51] Rockey DC, Barish M , Brill JV , et al . Standards for gastroenterologists for performing and interpreting diagnostic computed tomographic colonography. Gastroenterology 2007; 133 (3): 1005-1024 .

[52] Cash BD1, Rockey DC, Brill JV. AGA standards for gastroenterologists for performing and interpreting diagnostic computed tomography colonography: 2011 update. Gastroenterology. 2011 Dec;141(6):2240-66.

[53] Burling D; International Collaboration for CT Colonography Standards. CT colonography standards. Clin Radiol 2010; 65: 474-480.

Attendees are awarded a Certificate of Proficiency stating they meet the case requirement as specified in the ACR-SAR-SCBT-MR Practice Parameter for the Performance of Computed Tomography (CT) Colonography in Adults. Should the need arise, additional courses by academic groups, societies, industry, and ACR can be offered.

It has been shown that novice readers can achieve high sensitivity with formative training [54] and consistent expert level of interpretation with current display techniques can be achieved with continued experience[55]. The ability to compare performance across readers and across institutions is possible through participation in the ACR National Radiology Data Registry (NRDR) for CTC. The registry collects data across institutions to allow comparison of reader performance by comparing rates of true positives and detection of extracolonic findings.

Cost-Effectiveness

Cost-effectiveness analysis (CEA) studies are important to consider when discussing potential CRC screening options. These CEA studies, however, involve simulation models that are often complex and require careful review of the specific model inputs to ensure valid results. From a practical standpoint, it stands to reason that primary CTC with selective polypectomy should be more cost-effective than primary colonoscopy, as long as certain basic assumptions are met. One key assumption that was missing from the early CEA papers is that polypectomy should be avoided for isolated diminutive lesions seen at CTC.[56,57] The diagnostic performance of CTC should also reflect current practice and the input cost for CTC should be considerably less costly than colonoscopy. Ideally, extracolonic assessment should be factored in as well.[58] In general, it is relatively straightforward to demonstrate that CTC is cost-effective compared with no screening,[59] but with realistic input assumptions it can also be shown to be more cost-effective than the more invasive endoscopic strategies.[60,61,62] Most CEA studies comparing CTC and OC assume equal

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[54] Dachman AH , Kelly KB , Zintsmaster MP , et al . Formative evaluation of standardized training for CT colonographic image interpretation by novice readers. Radiology 2008; 249(1): 167-177.

[55] Liedenbaum MH, Bipat S, Bossuyt PM, Dwarkasing RS, de Haan MC, Jansen RJ, Kauffman D, van der Leij C, de Lijster MS, Lute CC, van der Paardt MP, Thomeer MG, Zijlstra IA, Stoker J. Radiology. 2011;258(2):477-487.

[56] Hassan C, Pickhardt PJ, Pickhardt PJ, Kim DH. Cost-effectiveness of CT colonography

CT colonography: pitfalls in interpretation. Radiologic Clinics of North America 2013;51:89-97.

[57] Pickhardt PJ, Hassan C, Laghi A, Zullo A, Kim DH, Morini S. Cost-effectiveness of colorectal cancer screening with computed tomography colonography - The impact of not reporting diminutive lesions. Cancer 2007;109:2213-21.

[58] Hassan C, Pickhardt P, Laghi A, et al. Computed tomographic colonography to screen for colorectal cancer, extracolonic cancer, and aortic aneurysm. Arch Intern Med 2008;168:696-705.

[59] Hassan C, Pickhardt PJ. 51:89-97.

[60] Pickhardt PJ, Hassan C, Laghi A, Zullo A, Kim DH, Morini S. 109:2213-21.

[61] Hassan C, Pickhardt P, Laghi A, et al. 168:696-705.

adherence rates. However, given recent evidence that CTC could substantially increase participation in screening, nearly all CEA models would likely favor CTC if this input were adjusted.[63] Beyond the typical Markov modeling, other decision analyses have been applied to certain key aspects of CTC screening, such as the management of small (6-9 mm) polyps.[64,65] More recently, a study by Pyenson et al.[66] compared the cost of CRC screening with CTC versus OC in the Medicare population and found that CTC was 29% less expensive in the base-case scenario. This study concluded that CTC is a cost-effective CRC screening option for the Medicare population and will likely reduce Medicare expenditures for CRC screening.

Increase in Screening Rates with CTC as a Covered Screening Option

Evidence shows an increase in colorectal cancer screening rates with the addition of CT colonography as a covered screening option. In both the University of Wisconsin and Colon Health Initiative (CHI) Bethesda experiences, colorectal cancer screening adherence has been found to improve with the implementation of CTC[67,68,69,70]. As opposed to substituting one exam for the other, the addition of CTC to the current menu of CRC screening options increases overall screening compliance rates.

In 2013 a multi-institutional study at military teaching facilities was published that estimated the potential impact of Health Effectiveness Data and Information Set (HEDIS) measures for colorectal screening if CT colonography was included over a five year period from 2006 to 2010. Four navy, 10 army, and 3 air force facilities were evaluated. During this period, the vast majority

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[62] Pickhardt PJ, Hassan C, Laghi A, Kim DH. CT Colonography to Screen for Colorectal Cancer and Aortic Aneurysm in the Medicare Population: Cost-Effectiveness Analysis. American Journal of Roentgenology 2009;192:1332-40.

[63] Pickhardt PJ. CT colonography: does it satisfy the necessary criteria for a colorectal screening test? Expert Rev Gastroenterol Hepatol 2014;8:211-3.

[64] Pickhardt PJ, Hassan C, Laghi A, et al. Small and diminutive polyps detected at screening CT colonography: A decision analysis for referral to colonoscopy. American Journal of Roentgenology 2008;190:136-44.

[65] Pickhardt PJ, Hassan C, Laghi A, et al. Clinical management of small (6- to 9-mm) polyps detected at screening CT colonography: a cost-effectiveness analysis. AJR Am J Roentgenol 2008;191:1509-16.

[66] Pyenson B, Pickhardt PJ, Sawhney TG, Berrios M. Medicare cost of colorectal cancer screening: CT colonography vs. optical colonoscopy. Abdom Imaging 2015;40:2966-76.

[67] Pickhardt PJ, Taylor AJ, Kim DH et al. Screening for Colorectal Neoplasia with CT colonography: Initial experience from the 1st year of coverage by private payors. Radiology 2006;241:417-25.

[68] 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

[69] 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

[70] Cash B, 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.

of CTC studies were performed at National Navy Medical Center of Bethesda (NNMC, n=9,474) and Navy Medical Center of San Diego (NMCSD, n=1,006). At NNMC a dedicated program of CTC screening was integrated with colonoscopy through funding by the Colon Health Initiative. A subgroup analysis at these two sites was performed from the April 2010 action list, including 24,286 screening patients from ages 50-75 (56-58% men). Yearly HEDIS compliance at NNMC ranged from 42.0% to 67.5% without CTC and from 49.7% to 84% with the addition of CTC. Yearly HEDIS compliance At NMCSD ranged from 33.8-65.7% without CTC and from 33.9-67.7% with the addition of CTC. Overall this study demonstrated improved HEDIS compliance, upwards of 80-85% for colorectal cancer screening with the inclusion of CTC[71].

University of Wisconsin is one of the largest CTC screening programs in the country, after becoming the first private institution in the United States to have third party payor reimbursement starting in 2004[72]. At Wisconsin, a multi-disciplinary collaboration between radiology and gastroenterology has led to productive clinical and research efforts. Several studies have looked at the short and long term impact of CT colonography on overall screening rates[73,74,75]. The CTC program began in 2004 with a peak number of 387 CTC examinations performed in the third quarter of 2005 and 275 examinations in the last quarter of 2011[76]. Although endorsed by American Cancer Society in 2008, the negative NCD by Medicare and lack of endorsement of USPTF in 2008 may have led to mixed messaging and decreased referral rates for CTC. Counter to earlier models which predicted CTC could decrease colonoscopy rates by 9-22%[77,78], at University of Wisconsin screening colonoscopies increased from a mean of 555/quarter in 2003 to 2,382 in 2011. The overall number of colorectal screening examinations (screening and diagnostic colonoscopy and CT colonography exams) increased from 555/quarter in 2003 to 1,736 in 2011. CT colonography represented approximately 10% of the total 10,986 colorectal screening

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[71] Cash BD, Stamps K, McFarland EG, et al. Clinical use of CT colonography for colorectal cancer screening in military training facilities and potential impact on HEDIS measures. J Am Col Radiol 2013;10:30-36.

[72] Pickhardt PJ, Taylor AJ, Kim DH et al. Screening for Colorectal Neoplasia with CT colonography: Initial experience from the 1st year of coverage by private payors. Radiology 2006;241:417-25.

[73] Pickhardt PJ, Taylor AJ, Kim DH et al. 241:417-25.

[74] 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

[75] 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

[76] Benson M, Pier J, Kraft S et al. 21(4):391-395

[77] Hur C, Gazelle GS, Zalis ME et al. An analysis of the potential impact of CT colonography on colonoscopy demand. Gastroenterology 2004;127:1312-1321.

[78] Ladabaum U, Song K. Projected national impact of colorectal screening on clinical and economic outcomes and health services demand on gastroenterology. Gastroenterology 2005;129:1151-1162.

examinations performed in 2011. Overall CTC added an additional 900 to 1400 patients screened annually. This article predicted if there was coverage and capacity to provide CTC, an additional 7-10% of patients could be screened annually with CTC.

In addition to evaluation of colorectal screening rates, patient preference studies of patients who have undergone CT colonography examinations have consistently demonstrated positive responses. 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[79].

In a study of 1,417 adults undergoing CTC screening in three different settings including a community practice, academic center and military medical center, the top reason for choosing CTC was 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, 29.6% 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[80]. Respondents reported a very high satisfaction level with CTC, and those who had experienced both modalities indicated a preference for CTC over optical colonoscopy. These results suggest that CTC has the potential to increase adherence to CRC screening guidelines.

CTC represents a valuable option to patients for colorectal screening. Specific cohorts who are targeted are those patients with prior incomplete optical colonoscopy (often due to excessive colonic tortuosity), patients at risk to undergo colonoscopy (typically from anesthesia or bleeding risks) or patients at low risk of colorectal cancer (with or without compliance to undergo other testing). Minimally invasive exam, lack of conscious sedation and recovery time and ability to drive to and from the procedure, including return to work on the same day, help to drive down costs of CTC and may improve patient compliance.

[79] Moawad FJ, Maydonovitch CL, Cullen PA, et al. CT colonography may improve colorectal cancer screening compliance. AJR 2010;195:1118-1123.

[80] Pooler BD, Baumel MJ, Cash BD, Moawad FJ, Riddle MS, Patrick AM, Damiano M, Lee MH, Kim DH, Muñoz del Rio A, Pickhardt PJ. Screening CT colonography: multicenter survey of patient experience, preference, and potential impact on adherence. AJR 2012;198:1361-1366.

Summary

The CTC Coalition feels strongly that CTC is proven to be an effective tool for screening of asymptomatic patients for colorectal cancer. Significant peer-reviewed evidence on the efficacy and safety of CT colonography has been published on a regular basis (see attached bibliography). The USPSTF analysis shows that CTC definitively meets the bar for a recommended test in the CISNET microsimulations. We note that ***CISNET microsimulations show that CTC at 5 year intervals meets the criteria for a recommended test*** (page 23 of the CISNET technical report).

In 2008 the USPSTF determined that the evidence was insufficient to assess the benefits and harms of CT colonography as a screening modality for colorectal cancer (an "I" statement). Concerns were cited regarding the perceived limited availability of CTC performed by trained and experienced radiologists, the potential harms associated with evaluation of incidental findings, and the cumulative risks of radiation exposure. Since the time of that publication, multiple studies have been published to address these topics. The American College of Radiology and the International CTC Standards collaborative have developed CT colonography practice guidelines and quality metrics, as well as specifications around training and certification. Based on the conclusions from the 2015 Systematic Review the CISNET models assumed no complications due to CT colonography. In their base-case analysis, CT colonography screening every 5 years was included in the set of recommended strategies with age to begin screening of 50 and age to end screening of 75, assuming selection of a 10-year interval for colonoscopy screening. In this model, a CT colonography screening strategy provided 91-96% of the life-years gained with 10-yearly colonoscopy over the same age range, and required significantly fewer colonoscopies.

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. Providing patients an additional effective screening tool for colorectal cancer will save lives and as reiterated in the recent final USPSTF recommendations, the best screening tool, is the one that actually gets done.

The CTC Coalition respectfully request that CMS recognize CT colonography as a recommended test for colorectal cancer screening for adults ages 50-75 as a screening benefit under Medicare. We are committed to helping CMS facilitate a safe and effective screening program, as the USPSTF and literature concludes CTC as a recommended and medically appropriate screening CRC exam.

If you have any questions or comments, please contact Anita McGlothlin at 800-227-5463 ext. 4923 or via email at amcglothlin@acr.org.

Sincerely,

Colon Cancer Alliance (CCA)
Colon Cancer Coalition (CCC)

Prevent Cancer Foundation (PCF)
Society of Abdominal Radiology (SAR)
Society of Computed Body Tomography & Magnetic Resonance (SCBT-MR)
American College of Radiology (ACR)
Medical Imaging Technology Alliance (MITA)
BRACCO
iCAD

Cc: William T. Thorwarth, Jr, MD, FACR, Chief Executive Officer
Ezequiel Silva, III, MD, Chair, ACR Commission on Economics
Lincoln Berland, MD, FACR, Chair, ACR Commission on Body Imaging
Judy Yee, MD, FACR, Chair, ACR Colon Cancer Committee