Health Technology Assessment

Updated Public Comments and Responses for Computed Tomographic Colonography (CTC) or Virtual Colonoscopy

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Document updated to include additional public comments received after response deadline.

ICER RESPONSE TO PUBLIC COMMENTS

January 29, 2008

Steven D. Pearson, MD, MSc

Industry Association Comment Responses

Comment One Response: We appreciate the importance attached by many to the results that are expected to be published by the American College of Radiology Imaging Network's (ACRIN) clinical trial of CT colonography. ICER's review made note of the press release of non-peer reviewed results from this trial, and it is our opinion that these results, if they are confirmed in peer-reviewed publications, will solidify estimates of the test characteristics of CT colonography that are, in fact, quite similar to those identified by systematic review of the existing literature by ICER. Because ICER used criteria for technical specifications and interpreter training that helped identify "state-of-the-art" CT colonography, our results discount poor results obtained from some earlier studies. The ACRIN trial results, if confirmed, will lend positive weight to judgments of the generalizability of these better test characteristics across a broader set of practices and patient populations. Therefore, it is our judgment that it is not unreasonable to believe that the ACRIN trial results will not materially change the core estimates for test characteristics provided by the ICER review. And the initial results from the ACRIN trial will not shed further light on other key elements of our assessment, including the potential benefits, harms, and costs of extracolonic findings, or the long-term risks of radiation exposure.

Comment Two Response In regard to the comment about published reimbursement rates for CT colonography, since there is no national Medicare coverage of screening CT colonography, nor are there any national insurers which cover the procedure, we believe the most reasonable approach is to benchmark against Medicare reimbursement rates for abdominal CT, and to perform sensitivity analyses with reimbursed prices as reported by physicians in Wisconsin, the only part of the country where several private insurers do reimburse for screening CT colonography.

AdvaMed recommends that the ACRIN findings be included in the Clinical Committee's consideration. Based on inclusion criteria, ICER concluded that data that had not received peer review was inappropriate to include formally in our meta-analysis, but we did provide the press release with early results as additional information to our Evidence Review Group for their consideration. As stated above, we do not believe that the early results announced to date suggest a significantly different estimate of the test characteristics for CT colonography than that provided in the ICER review.

Provider Association Comment Response

We appreciate the thorough and thoughtful comments from the ACG on the ICER review. We provide our responses in the categories they provide in their letter:

1) Colorectal Cancer Screening and Polyp Size

We acknowledge that there is not complete consensus across physicians or physician specialty societies on the most appropriate option for the management of polyps < 10mm. Advanced adenomas have been the target of screening with colonoscopy, and the probability of progression to cancer is related to the size of the polyp. The majority of lesions < 10mm regress (Hofstad B, Vatn MH, Andersen SN, et al, Gut 1996;39:449-456.) Studies have also shown that the risk of cancer is considerably less than 1% in polyps ≤ 5mm and may be as low as 0.25%. Therefore, whereas screening guidelines are quite clear that polyps ≥ 10mm are a target for screening and should be removed if discovered, consensus is less clear on the harm-benefit ratio for detection and removal of smaller polyps. Our review of the literature and consultation with clinical experts suggested a growing comfort with evidence suggesting that the biopsy of diminutive polyps ≤ 5mm was not likely to provide a net health benefit. As was stated in an American of Gastroenterology future trends report: "Polyps ≤ 5mm in size do not appear to be a compelling reason for colonoscopy and polypectomy, although the presence of multiple (≥ 3) small polyps might warrant colonoscopy." Considering the fact that leading practitioners of CT colonography follow the ACR reporting protocols that do not report polyps ≤ 5mm, and that some other accepted screening modalities for colorectal cancer, such as FOBT, are extremely unlikely to detect indirectly the presence of small polyps, the ICER review team felt it was appropriate to focus our evidence review on CTC performance for the detection of polyps > 6mm.

The ICER review does evaluate evidence separately for the performance of CTC to detect polyps 6-9mm and those ≥ 10mm. Our review therefore does not fail to address the implications of CTC performance in the management of polyps 6-9mm. Both our systematic review, meta-analysis, and economic modeling look specifically at the detection and management of polyps 6-9mm.

2) CTC Complications

The ACG has found an inconsistency in our report which we are glad to correct. The largest pooled result from CTC procedures in the US demonstrated two perforations out of more than 21,000 examinations; one of these was completely asymptomatic and was managed by observation only (Pickhardt PJ. Radiology 2006;239:313-316.) The Buring study mentioned in the ACG comment reported a 0.03% symptomatic perforation rate. Both of these complication rates are much lower than that generally reported for colonoscopy – 0.13% (Buring); 0.06% (Levin TR, Zhao W, Conell C, et al. Ann Intern Med 2006;145:880-886.)

The economic modeling performed as part of the ICER review did include the risk of perforation for colonoscopy and polypectomy of patients with positive CTC findings.

3) Patient Acceptance

The ICER review did not focus on differences between racial groups in acceptance of CTC vs. colonoscopy. The single article mentioned in the ACG comments suggests that over 80% of patients who underwent CTC would be willing to do so again. The data do not imply that introduction of CTC in addition to optical colonoscopy as an option for screening for colorectal cancer would reduce access to screening for minorities.

4) New Methods of Bowel Preparation

Because the development of a non-cathartic prep was known by several members of the ICER Evidence Review Group, we felt it appropriate to inform all members equally of clinical opinion that data this approach would be available within approximately one year. The review did not imply that the data would show favorable results, and we agree that current standards outside of clinical investigations are for the use of cathartic preparations.

5) Economic Modeling

The CISNET model used in this review does not dismiss all polyps < 6mm as hyperplastic. The model only simulates adenomas by size, and not by histology, therefore the model simulates the possible growth of polyps < 6mm into larger polyps, some of which will eventually develop into cancer.

We are unaware of data suggesting a better cost estimate for CTC than that used in this review. Knowing that CTC is not broadly covered by insurers, our review highlights that the relative price of CTC in relationship to optical colonoscopy has a strong role in assigning an incremental cost-effectiveness ratio for CTC. If CTC is being compared to no screening, the cost-effectiveness ratio per life-year gained is not very sensitive to the price of CTC.

We are unaware of data suggesting that “30% or more” of asymptomatic patients in a general screening population undergoing CTC might be sent for conventional colonoscopy. This may assume that patients with polyps < 6mm are referred for colonoscopy, but, as we have discussed above, this does not fit with current CTC protocols. In the largest US cohort to date (Kim et al, NEJM 2007;1403-1412), 12.9% of patients randomized to CTC had initial positive findings.

In regards to “false positive” rates, the ICER review estimates a specificity of 80%, lower than that in the pre-publication ACRIN trial (86%). Even with our lower specificity estimates built into the economic model, for every 1,000 patients screened with CTC there will only be 15 patients (1.5%) of patients with a “false positive” polyp seen on CTC.

6) Radiation Risk

We agree with the ACG comments that it is important to consider radiation exposure and its possible health effects. Experts believe it is a challenge to define precise risk estimates related to low doses of radiation exposure. In our report we sought to place the approximate mean individual does for CTC in the spectrum of other radiation exposure scenarios. As shown in our review, at current low-dose protocol levels, CTC radiation exposure is less than a plain lumbar spine x-ray, and less than one tenth of a traditional adult abdominal CT scan. Even if we were to frame our concern on the radiation exposure level of an abdominal CT scan, as the ACG comments note, this radiation has been estimated to cause 1 additional lifetime case of cancer or leukemia among 1,000 patients, whereas the overall risk of such cancer or leukemia is 420 in 1,000. We would add here that our model estimates that the number of colorectal cancer cases *prevented* with CTC screening is 53 for every 1,000 patients screened.

7) Miscellaneous Comments

We have changed all references to CTC to indicate that it is a "minimally non-invasive" test.

We agree that the criteria we used to identify relevant literature for our meta-analysis are very important in judgments about the accuracy of CTC. The probability that these standards can be achieved in the community is mentioned in our review as an important consideration. We also agree with the ACG that we did not hold optical colonoscopy to that same standard. Significant evidence exists of variation in the technical expertise of those performing optical colonoscopy, but we did not include consideration of this evidence.

CTC Public Comments – HTA Program Responses

DATE: Jan. 31, 2008

FROM: Leah Hole-Curry, Director HTA

Background

The HTA program selects health technologies to go through an independent review process. HTA posts information about selected health technologies for public comment at various stages. For Computed Tomographic Colonography (CTC), HTA received three comments from provider and industry associations in response to the posting of the draft evidence report. Some of the comments were program related not report related. Those program related comments are summarized and responded to below. Report related comments are responded to separately by the technology assessment vendor.

Comments

1. Timeline

   Comment: Two commenters were concerned about the timeline for this technology's draft key questions, draft report, and presentation to the clinical committee. The commenter's felt that there was insufficient time to respond in substance and that the program did not have adequate time to fully assess the technology.

   HTA Response: Both adequate stakeholder input and careful consideration of the technology by the clinical committee are critical to the program. Each technology includes at least one initial 30 day public comment period, followed by additional comment periods on key questions, draft reports, and to the clinical committee. The full CTC related timeframe and process steps are included below. In brief, CTC was announced in August 2007 with a solicitation for input open for 35 days, followed by two week comment periods after publication of key questions in December 2007, and the draft report in January 2008, and will finalize with comments to the clinical committee on February 15, 2008.

2. Report Selection

   Comment: One commenter was concerned that the report being issued within a weeks of the finalization of key questions did not allow the program adequate time to assess public comments received on key questions nor to adequately assess the data about the technology and write the report.

   HTA Response: The comment likely results from an incomplete understanding of the HTA process. HTA begins a review of a selected technology after the initial 30 day solicitation for input has closed. HTA drafts key questions intended to ensure that the report produced by our vendor will address program and committee mandates related to evidence about whether the technology is safe, effective, and cost-effective. Prior to finalizing the key questions, HTA posts them for public comment to ensure that significant issues were not missed.

   For CTC, all pubic comments received were considered. Minor adjustments to the key questions were made. Some comments were not consistent with the

program's mandates while others were substantive responses to the key questions, rather than comments about appropriateness of the key questions. The HTA is required to have an independent vendor produce the technology assessment report. HTA was able to identify that our key questions aligned with a recently produced systematic review and a new report was unnecessary. The HTA draft report, being an already existing product did not need extensive preparation time. Details on the methodologies used by the vendor to search and assess the evidence are documented within the report.

Project Title: CT Colonography for Colorectal Cancer Screening

The HTA is a program based on an innovative new law that promotes good health outcomes and cost effective care by paying for health technologies that are proven to be safe, effective and cost-effective. The main tool used to determine whether a technology is safe and effective is an independent systematic analysis. This report forms the basis for answering the primary policy question posed to a separate and independent provider committee: whether or not CTC should be covered, and under what conditions, if any.

1. Project Overview

Colon cancer is the nation's second leading cause of cancer deaths, and an estimated 52,000 people will die from it this year. Screening can save lives by finding growths before they turn cancerous. Colonoscopies, considered the gold standard test, are recommended every 10 years for everyone over 50 and more frequently after polyps are found or for high risk individuals. Only about one-half the population gets the recommended screening.

Traditional colonoscopy involves taking laxatives to cleanse the bowel and sedation for the procedure. A tube is inserted in the rectum and snaked through the large intestines by a gastroenterologist. Generally, any polyps that are spotted, regardless of size, are taken out in the process. Computed Tomography Colonoscopy (CTC) has been proposed as a less invasive alternative to screen for colorectal cancer, with a potential to increase the number of individuals screened. CTC involves taking laxatives to cleanse the bowel and inflating the colon (with air or gas using a small tube inserted in the rectum). A CT scanner is used to take a series of X-rays of the colon and a computer to create a 3-D view. A radiologist then checks the images for suspicious polyps. If any polyps need to be removed, the patient must then have a regular colonoscopy.

CTC Timeline

Milestone	Posted and Notice to Stakeholders	Comments Request Due
Preliminary List of Technologies	08-14-07	08-21-07
Technologies Selected For Review	08-27-07	10-04-07
Draft Key Questions	12-21-07	1-04-08
Final Key Questions	1-7-08	N/A

Draft report	1-11-08	1-25-08
Final Report	2-1-08	N/A
Comments Prior to Meeting Due	2-11-08	2-11-08
Clinical Committee meeting – Technology on Agenda (public comment at meeting permitted)	2-15-08	2-15-08

2. Key questions for investigation

1. What is the evidence to describe sensitivity, specificity, and other key test characteristics of CTC compared primarily to optical colonoscopy, but also in the context of the test characteristics of accepted modalities of colorectal cancer screening.
2. What is the evidence related to test characteristics of CTC variance according to the type of scanning machine and software, bowel preparation, reader training, and other operational factors?
3. What is the evidence about patient attitudes and acceptance of screening between CTC and colonoscopy?
4. What is the evidence about the cost impact of CTC?

To the extent that information was found on the following topic, it will be summarized, though it was not a primary question investigated in the already produced report.

- What is the evidence about patient characteristics that influence benefits and harms of CTC over usual cancer screening?
- Summarize clinical guidelines and CMS coverage policy and include the guidelines in appendices.

3. Commissioning of Report

After selection, HTA solicits public comment for at least 30 days. HTA also gathers information on what current policies, guidelines, and systematic reviews are available. For CTC, HTA program staff identified that the Institute for Clinical and Economic Review (ICER), had just completed a systematic review (October 2007) on CT Colonography for colorectal cancer screening. After the initial key questions were developed and comments received, they were compared against those questions investigated in the ICER report. Utilizing an existing review promotes the effective utilization of state resources, makes the program more efficient, and preserves flexibility in responding to Washington's unique needs as the author agreed to review all comments and revise the report to address program and stakeholder input.

Public Comments

VIA ELECTRONIC MAIL

January 25, 2008

Mr. Steve Hill

Administrator, Washington State Health Care Authority

Health Technology Assessment Program

P.O. Box 42712

Olympia, WA 98504-2712

RE: Assessment Process for Virtual Colonoscopy

Dear Administrator Hill,

The Medical Imaging and Technology Alliance (MITA) appreciates the opportunity to submit comments regarding the coverage of Virtual Colonoscopy to the Washington State Health Technology Assessment Program (SHTAP), as well as comments regarding the process by which this technology has been evaluated, thus far. As the leading trade association representing companies who represent over ninety percent of the global market for medical imaging, we hope that the SHTAP will consider these comments and our concerns regarding the overall assessment process.

Since the introduction of virtual colonoscopy (VC) on the market, numerous clinical studies have been performed praising the clinical outcomes of VC for certain patient populations and indications. These studies have shown that VC is a faster and more convenient procedure for the patient, offering a less intensive preparatory regiment and allowing patients to return to work the same day of the test since anesthesia is, generally, not needed. However, other studies have cited concerns over the accuracy of VC versus optical colonoscopy, particularly with polyps less than 5 millimeters in size. While these small polyps pose minimal risk of developing into cancerous tissue, the rate of detection with VC is slightly lower than traditional colonoscopy. Additionally, we understand there are concerns about the risk of bowel perforation in VC procedures. However, this risk is much higher for the more invasive optical colonoscopy, which is currently considered a necessary tool for colon cancer screening.

With these arguments to consider, MITA strongly encourages the Washington State Health Technology Assessment Program to postpone determination of a coverage decision until the American College of Radiology Imaging Network's clinical trial results and cost effectiveness data on virtual colonoscopy are published in a peer-reviewed journal for consideration. We have reviewed the ICER analysis and are concerned that the cost effectiveness component is based on the opinion of a technology assessment group and not on published literature. We

understand that the goal of the SHTAP is to promote evidence-based utilization; using an assessment that conflicts with published literature/evidence appears to contradict this goal. For example, the latest published reimbursement rate for VC was not used in the cost effectiveness analysis, which raises considerable concerns as to the accuracy of the analysis.

MITA is also troubled with the timeline and process by which this technology has been evaluated. We were asked on December 21, 2007 to publicly comment on the key questions used to assess this technology. Two weeks later, the ICER report was issued. We are struggling to understand the purpose of commenting on such key assessment questions if the SHTAP was not intending to utilize them when compiling the assessment.

MITA understands that a meeting is scheduled on February 15 to issue a final decision on VC. This allows only one month for the SHTAP to fully assess the technology, without considering the ACRIN study data, the most highly regarded data on this subject. The SHTAP website states that two to six months will be dedicated to a full review of each technology. MITA believes that the hurried nature of this review undermines the guidelines laid out for the Program and does not provide adequate time to fully assess clinical data for this valuable technology. Due to the concerns above, MITA strongly urges the SHTAP to withhold issuing a final decision on VC and appoint a technical advisory committee to convene after the February session to look at latest health economics and clinical results, in depth MITA would be interested in meeting with you to discuss our concerns about the assessment process further. In the interim, we strongly advise the STHAP to postpone coverage determination until the results of the ACRIN study have been published and analyzed by medical professionals. MITA appreciates the State Health Technology Assessment Program's consideration of the above recommendations. Should you have any further questions or comments, please do not hesitate to contact me at tgorenc@medicalimaging.org or 703-841-3247.

Sincerely,

Theresa M. Gorenc

Director, Health Policy

Leah Hole-Curry, JD

Director, Health Technology Assessment

Washington Health Care Authority

Olympia, WA

Dear Ms Hole-Curry:

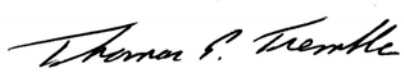
On behalf of members of the Advanced Medical Technology Association, AdvaMed, I want to share our concerns with the assessment for Virtual Colonoscopy. It appears that the CTC assessment is being rushed through to meet an arbitrary timetable, which will not serve the best interests of patients. Among the signs of a rush to judgment:

- Late in the day on December 21, the HCA issued draft questions, with comments due on January 4, 2008. While it is important for the HCA to conduct its work in a timely manner, it is implausible to think that during that time period many stakeholders would be focused on technology assessment questions and be able to prepare more than a cursory response. Then, the draft report was released on January 11, with only a two week comment period.
- As the first assessment scheduled for 2008, it would be completed prior to publication of the final results of a definitive study of Virtual Colonoscopy; the American College of Radiology Imaging Network (ACRIN) study. Under the HCA processes, reconsideration of the technology to incorporate greater consideration of the ACRIN study would not take place until eighteen months.
- Page seventeen of the draft report references the ACRIN study. The citation notes that preliminary findings were released in September and that a website report is enclosed as an attachment. However, since the report of the findings was not attached, assessment commenters are unable to comment on the ACRIN study.

Due to the ACRIN report's significance, as indicated in the draft assessment, we strongly urge that the ACRIN findings be included in the Clinical Committee's consideration by either postponing the CTC assessment until the ACRIN findings are finalized and published or convening an advisory committee that would be able to take into account the preliminary ACRIN findings.

I appreciate your consideration of our concerns.

Sincerely,



Thomas E. Tremble

Associate Vice President, State Government Relations

January 24, 2008

Denise C. Santoyo
Program Coordinator
Office of Health Technology Assessment
Washington State Health Care Authority
P.O. Box 42700
Olympia, Washington 98504
Submitted via e-mail to: shtap@hca.wa.gov

Dear Ms. Santoyo:

On behalf of the American College of Gastroenterology, including some 200 members in Washington State, we would once again like to provide expert commentary to aid in your agency's assessment of Virtual Colonoscopy/Computed Tomographic Colonography (CTC). We provided preliminary guidance on CTC to your agency in the first-round of information gathering as well as on the questions posed in December. At this time, we would like to comment on the Health Technology Assessment (HTA) conducted by the Institute for Clinical and Economic Review dated January 11, 2008. While it is an impressive study, we have several concerns about its findings, and as a leading specialty society the College believes that clinical evidence must inform reimbursement and technology assessment decisions.

Colorectal Cancer Screening and Polyp Size

As we commented previously, small polyps cannot be ignored. We are concerned that this evidence review chose to ignore the performance of CTC for polyps less than or equal to 5 millimeters. There is ample evidence to show the clinical significance of such polyps.

First, the National Polyp Study has shown that three adenomas of any size is the most consistent predictor of an advance adenoma, and 80% of all adenomas are < 6mm. Furthermore, in a recent analysis of the extensive colonoscopy database at Indiana University by Dr. Doug Rex, 30% of all patients with high risk adenomas as defined by post-polypectomy surveillance were patients with 3 adenomas less than 6 mm in size and no polyp of any histology 6 mm or larger. Hence it is problematic to dismiss polyps based on size or infer that polyps < 6mm are inconsequential.

Second, a recent study (Butterfly et al Clin Gastroenterol Hepatol 2006;4(3): 343-48) emphasized the prevalence of clinically important histology in small adenomas. Data were reviewed retrospectively from 3,291 colonoscopies performed on asymptomatic patients found to have an adenoma on screening with flexible sigmoidoscopy a few weeks before the colonoscopy or who had a family history of colorectal cancer. All polyps were excised endoscopically and sent for pathology testing. Specimens with advanced histology were confirmed by a second reading. Of the 3,291 colonoscopies performed, 1,235 yielded a total of 1,933 small or diminutive adenomatous polyps.

Advanced histology including carcinoma was found in 10.1% of small (5–10 mm) adenomas and in 1.7% of diminutive adenomas (≤4 mm). Carcinoma was found in .9% of small adenomas, and 0% of diminutive adenomas.

It addition to ignoring small polyps generally, the report also specifically fails to address the implications of dismissing small polyps found by CTC. A recent decision analysis (Hur et al. Clin Gastroenterol Hepatol 2007; 5(2): 237-244) addressed this issue. The authors reported that if CTC

is used for colorectal cancer screening, the majority of polypoid lesions identified will be less than 10 mm in size. Decision-analytic techniques were used to compare the outcomes of 2 management strategies for smaller (6–9 mm) polyps discovered by CTC. Hypothetic average-risk patients who had undergone a CTC examination and found to have a small (6–9 mm) polyp were simulated to either: (1) undergo immediate colonoscopy for polypectomy (COLO), or (2) wait 3 years for a repeat CTC examination (WAIT). A Markov model was constructed to analyze outcomes including the number of deaths and cancers after a 3-year follow-up period or time horizon. Values for the model parameters were derived from the published literature and from Surveillance Epidemiology and End Results data, and an extensive sensitivity analysis was performed. The colonoscopy strategy resulted in 14 total deaths per 100,000 patients compared with 79 total deaths in the WAIT strategy, for a difference of 65 deaths. The colonoscopy strategy resulted in 39 cancers per 100,000 patients vs. 773 in the WAIT strategy, for a difference of 734 cancers. Sensitivity analysis found that model findings were robust and only sensitive at extreme parameter values. The study concluded that managing smaller polyps detected on a screening CTC with another CTC examination 3 years later likely will result in more deaths and cancers than immediate colonoscopy and polypectomy.

CTC Complications

We would like to alert you to some inaccuracies and incomplete analyses in the discussion of potential harms of CTC. For instance, the current draft states, that CTC has "a far lower rate of complications than colonoscopy, due to absence of risk of perforation (0 per thousand vs. 0.7 per thousand.)" In fact there are two extremely large studies involving CTC that cite a perforation rate comparable to optical colonoscopy (Sosna J et al. Colonic perforation at CT colonography: Assessment of risk in a multicenter large cohort. Radiology 2006 May; 239:457-63.
Burling D et al. Potentially serious adverse events at CT colonography in symptomatic patients: National survey of the United Kingdom. Radiology 2006 May; 239:464-71)

Recognizably also the number of complications for colonoscopy encompasses all diagnostic and therapeutic procedures (polypectomy), hence these complications need to be put in perspective also against alternative intervention (surgery) vs. no intervention as well as distinguish between screening and diagnostic colonoscopy. In the first study, researchers reviewed data from 11,870 CTC studies performed at 11 centers in Israel during a two-year period. These studies represented more than 95% of all CTC studies performed in Israel during this interval. Seven perforations occurred, yielding a rate of 1 in 1700 (0.06%). Five perforations occurred in the sigmoid colon and two in the rectum. Four patients required surgical treatment.

In the second study, researchers interviewed the lead gastrointestinal radiologists at 50 centers in the UK to determine the number of CTCs ever performed and the number of perforations. Of 17,067 patients who underwent CTC, 9 had perforations (1 in 1900 or 0.05%). Overall, the perforation rate among symptomatic patients in these studies ranged from 0.03% (1 in 3400 patients) to 0.06% (1 in 1700 patients). These rates are much higher than those seen with barium enema and, for many individual endoscopists, exceed the rates of diagnostic perforation during conventional colonoscopy.

Patient Acceptance

The executive summary states that "….among patients who experienced both CTC and colonoscopy, a small majority preferred CT colonoscopy." This statement may ignore key subpopulations. For instance, there is a recent report suggesting a bias a minorities AGAINST

CTC compared to colonoscopy. This might be important to acknowledge given the disparity of CRC instance, there is a recent report suggesting a bias a minorities AGAINST CTC compared to colonoscopy. This might be important to acknowledge given the disparity of CRC screening in the US for minorities. (Roshini et al. Clin Gastroenterol Hepatol 2007; Aug 3). This is important as racial/ethnic minorities are less likely to undergo CRC screening than whites. Racial/ethnic minorities were significantly less likely than whites to prefer CTC over OC (whites, 65.7%; blacks, 45.1%; Hispanics, 35.8%; and other, 35.7%; P < .001). Racial/ethnic minorities were less satisfied with CTC (whites, 8.4 +/- 1.7; blacks, 7.8 +/- 1.7; Hispanics, 7.4 +/- 1.8; and other, 7.5 +/- 2.1; P = .001) and were significantly less willing to undergo CTC again in the future (whites, 95.5%; blacks, 80.3%; Hispanics, 84.9%; and other, 85.7%; P = .006). Compared with white patients, colonoscopy was better tolerated and preferred over CTC for evaluation of the colon among racial/ethnic minorities. Given the serious challenges we face in this country with healthcare disparities including in access to CRC screening, this data should not be ignored.

New Methods of Bowel Preparation

The discussion (see page 9 of the report) states "on the horizon there is new method of bowel prep for CTC and this is a non-cathartic, and if this method is demonstrated to provide the same sensitivity/specificity as current CTC, patient acceptance of CTC is likely to be much higher than for colonoscopy. Our clinical experts estimated that evidence on the performance of non-cathartic prep would be available within the next 9-12 months." We would suggest that, from an evidence-based review based on published data, that this assertion is conjectural and inappropriate. A non-cathartic approach to CTC (Mayo Clin Proc 2007;82:666-71) suggested that preparation for CTC was in fact necessary for optimal utilization – if CTC was to be done. The absence of a cathartic prep would preclude same day colonoscopy. The greatest aversion for a cathartic prep was from prior exposure. Most importantly-the majority of data and all the data on screening with CTC has been with a cathartic based preparation.

Economic Modeling

The College is concerned that, as the report states, "The economic model does not explicitly simulate hyperplastic polyps." (page 10) The assumption for that model was based on size and not histology. Dismissal of polyps <6mm as hyperplastic is conjectural as to the actual histology and not an accurate assumption.

CTC is an expensive examination, being at least five times more expensive than the current radiographic imaging test for colon polyps, double contrast barium enema.

30% or more of patients undergoing CT colonography in many centers might be sent for conventional colonoscopy for false positives. These specificities are indeed lower than what has been traditionally reported for double contrast barium enema. In one large study of CT colonography, 197 of 300 patients had a true or false positive polyp (Yee, Radiology 2001;219:685-92). The recent abstracted report from the ACRIN trial cites a specificity of 86% for reportable polyps. This means that over a ten year period, at least 42% of patients would be referred for a colonoscopy. This was not the assumption used in the present cost modeling for discussion of cost effectiveness. Additionally, earlier follow-up for smaller polyps was not built into the logic of the assumptions; hence these cost modeling data are very misleading.

Radiation Risk

The College is troubled that the discussion of radiation exposure and future cancer risk that begins on page 34 of the report inappropriately diminishes the risk of radiation exposure

associated with abdominal CT imaging. Conservative estimates are that more than 60 million CT examinations were done in 2002 in the USA, representing an estimated 70% of all medical X-ray exposure. (OW Linton and FA Mettler Jr, National conference on dose reduction in CT, with an emphasis on pediatric patients, AJR Am J Roentgenol 181 (2003), pp. 321–329) Although it is a challenge to define precise risk estimates related to low doses of radiation exposure, the ionizing radiation exposure from a single abdominal or chest CT may be associated with elevated risk for DNA damage and cancer formation (M Lobrich, N Rief and M Kuhne et al., In vivo formation and repair of DNA double-strand breaks after computed tomography examinations, Proc Natl Acad Sci USA 102 (2005), pp. 8984–8989.) The seventh National Academy of Science report on Biological Effects of Ionizing Radiation (BEIR) is the most recent update from a respected organization. (Committee to Assess the Health Risks from Exposure to Low Levels of Ionizing Radiation, BEIR VII: health risks from exposure to low levels of ionizing radiation (nhttp://www.nap.edu/reportbrief/11340/11340rb.pdf) BEIR VII indicated that a single population dose of 10 mSv is associated with a lifetime attributable risk for developing a solid cancer or leukemia of 1 in 1000. The overall risk for developing a solid cancer or leukemia from all causes would be 42 in 100.

The radiosensitive tissues are predominantly within the field of view of common chest, abdominal, and pelvic CT scans: the typical abdominal examination dose is between 10 and 20 mSv. Unfortunately many patients are exposed to multiple examinations that increase cumulative dosing. A recent report focused on the effects of multiple exposures to ionizing radiation during CT. They found that a subset of patients with renal colic commonly had total exposure rates between 19·5 and 153·7 mSv (SI Katz, S Saluja, JA Brink and HP Forman, Radiation dose associated with unenhanced CT for suspected renal colic: impact of repetitive studies, AJR Am J Roentgenol 186 (2006), pp. 1120–1124)

Radiation effects may not manifest until 5–20 years after the scan, and causal relations are unapparent on an individual basis.

The US Food and Drug Administration has listed medical X-rays as a known carcinogen. It may be necessary for governments to place guidelines on acceptable maximum doses and indications for CT. For instance, questionable practices such as whole-body CT screening examinations that expose normal individuals to known risks with unknown benefits might need to be restricted.

Cross-sectional imaging has revolutionized diagnosis and medical practice in the past 30 years. Clinicians, as patients' advocates, are obliged to understand and explain the risks associated with CT radiation, and to provide state-of-the-art dose-reduction techniques,

X-rays used in medical diagnostic procedures is the largest man-made source of radiation exposure to the population, contributing with some 14% of the total annual exposure from all sources. Ionizing radiation from diagnostic procedures has been postulated to cause several hundred cases of cancer per year in the UK (AB de Gonzales and S Darby, Risk of cancer from diagnostic x-rays: estimates for the UK and 14 other countries, Lancet 363 (2004), pp. 345–351)

It is, however, reasonable to assume that many health professionals underestimate the potential hazard of ionizing radiation in common diagnostic procedures. The authors should also discuss the implication of obesity on dosimetry requirements for these exams. Obesity (60 million US; 30% of population) increases the dosimetry for accurate CT imaging, approximately by a factor of 2. Hence the impact of repeated higher dose exposures for these patients over time may be even more important- in a patient group that already has a higher associated risk for many intra-abdominal cancers.

Miscellaneous Comments

The report's introduction refers to CTC as "non-invasive," which is a suboptimal choice of phraseology as CTC requires prep, rectal tube insertions/air insufflations, radiation exposure and in many studies the use of intravenous medicine.

With regard to the report's methodology which on page 29 states that the review identified four components of CTC "using the best technology and performance standards," we would point out that the comparison of optical colonoscopy is not held to the same standards, and in the real world, it is likely that CTC would not always be done consistently with these criteria.

We appreciate the agency's collaborative and transparent approach to technology assessment thus far on CTC and appreciate the opportunity to comment on the ICER review. Please don't hesitate to contact me or Julie Cantor-Weinberg, the ACG's Vice President of Public Policy, if we can clarify any responses or provide you with any additional information.

Respectfully submitted,
Amy Foxx-Orenstein, D.O, FACG
President

Additional Public Comments

Note: Comments received after public comment deadline are included for consideration, but not responded to by the technology assessment center.

-----Original Message-----
From: Patrick Price, Wheatlands Administrative Services

I would like to submit the following comment on the excellent analysis of virtual colonoscopy by the Washington Health Technology Assessment group. I believe the comment will be accepted through today January 28, 2008. The authors, doctors, are the following:
January 1, 2008
Roberta Scherer, PhD
Amy Knudsen, PhD
Steven D. Pearson, MD, MSc

The link to the document is the following:
http://www.hta.hca.wa.gov/reviews/

The objective of the Washington Health Technology Assessment is to determine if CT colonoscopy, virtual colonoscopy (VC) is a good substitute for optical colonoscopy (OC). There are two premises of the thorough scientific analysis by the authors which might be considered from a different perspective. First because colorectal cancer is the second leading cause of cancer related deaths in the United States the patient should know the negative predictive value (NPV) of the two tests. The polyps missed are of more potential harm to the patient than those correctly detected. Intuitively patients will understand that they want to know the level of assurance they have they are disease free. If the results of the test show they are not at risk for colon cancer how confident can they be the prediction is correct. Furthermore, patients individually will be concerned about polyps greater than 6mm (>6mm) if they know individually there is 2-7% chance their polyp will have high grade dysplasia. In order to calculate the negative predictive the prevalence in the tested populations should be the same. So the studies that used some patients that have symptoms for example melana are not as useful in calculating the NPV as the studies which use only asymptomatic individuals because the prevalence of the disease in asymptomatic individuals is the same as those being screened using OC. Using the pooled data including the Rockey study on page 53 the NPV is 93.5%. Patients should know 6:100 may have a dysplastic polyp if VC is chosen in place of OC. Personally I have undergone OC without anesthesia and this is the follow-up procedure I will select in the future. I want the best odds of success; in other words as an individual patient I am interested in superiority not the existence of non-inferiority in detection of colon cancer.

Next, I would like to suggest more scrutiny be given to those instances when contrast is used. Medicare patients may have several comorbidities like diabetes and hypertension plus factors like age which all contribute to the risk of acute renal failure when contrast is used. The study by Barrett et al analyzes this problem and implies that it may be under estimated. The article includes a good risk calculation table and for those tests which use contrast this article offers useful facts to consider.

Barrett BJ,

Parfrey PS
Prevening nephropathy induced by contrast medium
N Engl J Med (2006); 354:379-86

Finally, the increasing use of computed tomography for evaluation of other organ systems and the number of cumulative mSev of radiation over time should be considered in addition to the context of one scan and 5 or 10 mSev. The radiation dose is cumulative. Therefore, and argument can be put forward to consider that the avoidance of radiation when another means of testing is available is desirable.

I have extracted some narrative from the very comprehensive and clear document by the authors of the Washington State Health Assessment of virtual colonoscopy followed by the page numbers below. The table on page 53 with the pooled data I relied upon to determine my estimate of the NPV I could not paste in a readable format. The other material points up information I believe support detecting polyps > 6mm. Furthermore, I wanted to point out that the prevalence of extracolonic cancers detected by VC of 3:1000 on page 33 may not offset the fact that VC may miss 6:100 6mm or greater dysplastic polyps in the decision making process of a patient. So can this be offered as a potential benefit of VC? I offer the same point about the reduction of bowel perforation of 0.05% or 5:10,000 when VC and OC are compared for this untoward effect. Statistics are provided due to the author's research on page 34.

The only reason that I include the cost analysis is to contrast the assessment of cost with the evaluation of what approach has the highest likelihood of detecting adenomatous polyps and not missing polyps which may lead to cancer. The best approach should be covered. A non-inferior approach should be accepted or reimbursed if there are mitigating circumstances.

Guidelines for the management of polyps 6-9mm are less well defined. In polyps of this size, studies have indicated that 2-7% will contain high grade dysplasia and 0.9% will show invasive cancer (Van Dam 2004). A recently published decision analysis suggests that leaving these polyps in place results in 10-fold more cancers and 8-fold more deaths at 3 years, but investigators with Pickhardt's group in Wisconsin suggest that for patients with one or two polyps between 6-9mm it is reasonable to offer them the option of repeat CTC at 2-3 year intervals. Varying opinions are also expressed in the literature regarding the significance of "flat" polyps. In European populations, up to 36% of adenomas removed were found to be flat or depressed. Studies indicate that flat or depressed lesions may be present in uip to 22.7% of patients undergoing screening colonoscopy in the United States (Saitoh, 2001). Flat polyps have been reported to be significantly more likely to contain high-grade dysplasia that protuberant polyps (Tsuda, 2002). However, this remains controversial for U.S. populations. A reclassification of sessile adenomas identified at baseline in the National Polyp Study cobort into flat or polypoid adenomas, indicated that flat polyps were not associated with a higher risk for high-grade dysplasia initially or for advanced adenomas at surveillance (O'Brien, 2004). The importance of flat polyps in western populations, therefore, remains unclear. (22)

We also did not include any criteria related to the use of oral or intravenous contrast materials. Although use of contrast material may be considered an important component of current CT technology, it appears not to be routinely used as yet, with few studies reported using either type of contrast media. (29)

Similar results were obtained for analyses comparing CT colonography with colonoscopy for sensitivity for detection of adenomatous lesions. For lesions >10 mm, combining the results from five studies (Ginnerup 2003, Hoppe 2004a, Pickhardt 2005, Rockey 2005, Van Gelder (2004)

resulted in a pooled sensitivity of 81% (95% CI, 75-86%) for CT colonoscopy compared with 91% (85-94%) for colonoscopy. Although not a direct comparison, Iannaccone reported that colonoscopy missed 5 of 162 polyps, 4 to 8 mm in size (2004), and in a subsequent study colonoscopy failed to detect 16 of 94 polyps, 4 to 14 mm in size (Iannaccone 2005). (33)

In the largest series reported to date (Kim, 2007), 241/3120 (7.7%) of asymptomatic patients screened with CTC had an extracolonic finding that led to a recommendation for an additional test or procedure. Among these patients eight extracolonic cancers were seen, accounting for a prevalence of 0.3%. (33)

Harms associated with CT colonography have been reported, however. In a survey by Burling and colleagues of 50 institutions, nine cases of colonic perforation were reported in 17,067 CT colonographic examinations, a rate of 0.08% (Burling 2006). Similarly, in a survey of 11 medical centers, Sosna (2006) reported seven cases in 11,870 examinations (0.06%). It is important to point out that of the 16 instances of perforation, twelve occurred in patients with an existing colonic condition or disease (i.e.., irritable bowel syndrome, inguinal hernia, diverticulosis, etc.). By comparison, the rate of colonic perforation for optical colonoscopy is reported to be 0.13% (Burling 2006), significantly higher than that reported for CT colonography. (34)

The C/LYS of CTCM 5y compared to colonoscopy every ten years is highly sensitive to the procedure cost ratio (i.e., the ratio of the costs of a CTC and of a colonoscopy without polypectomy). In our base-case analysis with the costs of CTC and colonoscopy nearly identical ($523.40 for CTC vs. $522.47 for colonoscopy without polypectomy), the C/LYS vs. colonoscopy is over $600,000. However, if the procedure cost ratios are 0.52, 0.47, and 0.42 then the C/LYS of CTCM 5y vs. colonoscopy are $150,000, $100,000, and $50,000 respectively. Procedure cost ratios of this magnitude may be reasonable, given that the cost ratio at the University of Wisconsin Medical School, where CTC has been covered by several third-party payers since 2004,39 is 0.36. (74)