CENTERS FOR MEDICARE AND MEDICAID SERVICES

MEDICARE EVIDENCE DEVELOPMENT AND COVERAGE
ADVISORY COMMITTEE

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RE: SCREENING COMPUTED :
TOMOGRAPHY :
COLONOGRAPHY (CTC) :
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Woodlawn, Maryland

Wednesday, November 19, 2008

The above entitled matter came to be heard before the Medicare Evidence Development and Coverage Committee in the CMS Auditorium, 7500 Security Boulevard, Woodlawn, Maryland.

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P R O C E E D I N G S

MS. ELLIS: Good morning and welcome, chairpersons, members, and guests. I am Maria Ellis, an executive secretary for the Medicare Evidence Development and Coverage Advisory Committee, MedCAC.

The Committee is here today to discuss the evidence, hear presentations and public comment, and make recommendations concerning the screening computed tomography colonography for colorectal cancer for eligible individuals. The meeting will discuss the various kinds of evidence that are useful to support requests for Medicare coverage in this field.

The following announcement addresses conflict of interest issues associated with this meeting and is made part of the record. The conflict of interest statutes prohibit special government employees from participating in matters that could affect their or their employer's financial interest. Each member will be asked to disclose any financial

conflicts of interest during their introduction.

We ask in the interests of fairness that all

persons making statements or presentations also disclose any current or previous financial involvement in a company that manufactures or provides devices or other tools for the research of computed tomography colonography. This includes direct financial investments, consulting fees, and significant institutional support. If you haven't already received a disclosure statement, they are available on the table outside of the auditorium.

We ask that all presenters please adhere to their time limits. We have numerous presenters to hear from today and a very tight agenda and, therefore, cannot allow extra time. There is a timer at the podium that you should follow. The light will begin flashing when there are two minutes remaining, and then turn red when your time is up.

Please note that there is a chair for the next speaker, and please proceed to that chair when it is your turn.

For the record, voting members present for today's meetings are: Dr. Clifford Goodman, Dr.

Robert McDonough, Dr. Curtis Mock, Dr. Arden Morris, Dr. Gerald Peden, Dr. David Samson, Dr. Gurkirpal, Singh, Dr. Steven Teutsch, Dr. Jonathan Weiner, and Dr. Jed Weissberg. A quorum is present, and no one has been recused because of conflicts of interest.

The entire panel, including non-voting members, will participate in the voting. The voting scores will be available on our website following the meeting. Two averages will be calculated, one for voting members, and one for the entire panel. I ask that all panel members please speak directly into the mics. And you may have to move the mics, since we have to share.

If you require a taxicab, there's a sign-up sheet at the desk outside of the auditorium. Please submit your request during the lunch break. And lastly, please remember to discard your trash in the trash cans located outside of this room.

And now, I would like to turn the meeting

over to Dr. Steve Phurrough.

DR. PHURROUGH: Good morning. I'm Steve

Phurrough. I'm the director of the coverage and analysis group here, and I am the government liaison to this advisory committee. I'd like to welcome you here today. A special thanks to the panel members who have taken time out of their busy schedule to help us with this particular issue.

The Medicare Coverage Advisory Committee's role is to provide us recommendations as to what the evidence demonstrates around a particular issue that we are addressing. In this particular case, it's the use of CT colonography in the screening for colorectal cancer disease.

The purpose of this meeting is to discuss the evidence. It is not for the panel to recommend as to whether we should or should not cover this particular technology.

In general, the Agency has -- and I've stated in the past, we do not consider cost in making coverage decisions. However, Congress in passing the

20 legislation that authorized coverage for colorectal

21 cancer screening authorized us to look at the cost of

these particular technologies in the assessment of coverage of these different technologies. So we'll have that discussion today also as to the cost effectiveness of this particular technology.

Before going any further, I'd like to talk for just a moment and say a few words about Ron Davis. As many of you know, Ron Davis, the recent past president of the AMA, died earlier this month after a fairly short illness with pancreatic cancer.

Ron was chairman of this council for two years. Extremely professional, extremely well thought of in the prevention community, a real giant in that community. The community is better for Ron having been part of that. And I wanted to recognize him and offer our condolences to his family at this particular time.

With that, I'd like to turn the meeting over to Barbara and begin the discussion.

DR. MC NEIL: Thank you, Steve. What I'd

like to do before we start our formal presentation is

ask the panel members to introduce themselves. And

maybe we could start over there with Jed?

DR. WEISSBERG: Thank you. Jed Weissberg, Kaiser Permanente in California.

DR. WEINER: Jonathan Weiner from the Johns Hopkins School of Public Health here in Baltimore and also the School of Medicine.

DR. TEUTSCH: Steve Teutsch from Merck. I'll be retiring the end of the month and joining the L.A. County Health Department.

DR. SINGH: Gurkirpal Singh from Stanford University School of Medicine, Division of Gastroenterology and Hepatology.

DR. SAMSON: David Samson, the Blue Cross and Blue Shield Association Technology Evaluation Center.

DR. PEDEN: Gerald Peden with Independence Blue Cross.

DR. MORRIS: Arden Morris, Department of Surgery at University of Michigan.

DR. MOCK: Curtis Mock, Health Services, United Healthcare.

DR. MC DONOUGH: Bob McDonough from Aetna.

DR. GOODMAN: Cliff Goodman with Lewin Group.

DR. PEARSON: Steve Pearson, the Institute for Clinical and Economical Review at Mass General Hospital.

DR. MC NEIL: Barbara McNeil, Harvard Medical School and Brigham and Women's Hospital.

Thank you all. Could everybody hear Jed and Jonathan at the last microphone? Is that okay? It seemed a little low to me. But if it's okay -- is that all right? Just double check, would you, Maria? Okay?

So with that, I'd like to introduce Dr. Larson from CMS who will present TA that has been done for this purpose by our -- I'm sorry. I'm sorry. I'm running ahead of myself. He will present the questions that we will be answering later this afternoon.

DR. LARSON: Good morning. Can you hear me?

I'm Bill Larson from the Coverage Analysis Group.

Today's topic is a very important one, screening computed tomography colonography, also referred to as CTC or CT colonography or virtual colonoscopy for colorectal cancer.

On behalf of the project team and CMS leadership, I want to welcome the panel and everyone else to Maryland and the Centers for Medicare and Medicaid Services. We're happy to have you here and hope you don't mind the 26 degree weather here.

The panel has already received the following materials in advance of the meeting. First are the two Agency for Healthcare Research and Quality technology assessments. The first was a systematic review of the evidence that was prepared by the Oregon Evidence-based Practice Center. It was published in the Annals of Internal Medicine on November 4th, 2008.

The second is a draft cost effectiveness analysis of CTC screening that was prepared by the Cancer Intervention and Surveillance Modeling Network

or CISNET and was posted on the CMS website on November 12th, 2008.

We have also provided the panel with the presentations of our two TA presenters and our invited guests and statements of other speakers and related materials.

Finally, we have provided the panel with copies of the seven voting and five discussion questions that I will run through quickly in the next few minutes after providing some brief background information on the Medicare colorectal cancer screening benefit.

There was Medicare amendments of 1997 and 2001, where there were regulations that established a screening benefit for average risk individuals age 50 and over. There are four different types of tests; fecal occult blood tests, flexible sigmoidoscopies, colonoscopies, and barium enemas.

The Medicare law and regulations also provide that in addition to those tests, CMS is allowed to use the National Coverage Determination

process to add coverage for other types of colorectal screening tests as they determine to be appropriate.

So it is under that authority that CMS initiated the national coverage analysis on CTC screening earlier this year.

The specific legal authority that allows CMS to develop NCDs on new colorectal cancer screening tests is Section 1861(pp)(1)(D). That's the last chapter of the Social Security Act. We have used this authority several times in recent years to evaluate new screening options that have been brought to our attention.

For example, on November 4th, 2003, CMS issued a positive NCD on screening amino acidic fecal occult blood tests based on that authority after considering their risk factors, including sensitivity, specificity, safety, and cost effectiveness.

For the panel, voting questions. We are asking panel members to score on a rating scale of one, no confidence, to five, high confidence, their answers to the following voting questions:

Question number one, how confident are you that there is sufficient evidence to determine the

sensitivity and specificity of screening CTC using at least 16 slice scanners for average risk individuals compared to optical colonoscopy for polyps in three size categories, A, less than six millimeters, B, six to less than ten millimeters, and C, equal to or greater than ten millimeters?

Question number 2, how confident are you that there is sufficient evidence to determine the health benefits of screening CTC using at least 16 slice scanners for, A, polyps for less than six millimeters, B, polyps six to less than ten millimeters, and C, polyps equal to or greater than ten millimeters?

Question 3, how confident are you that previous evidence and modeling for the treatment of polyps discovered using other screening modalities can be applied to polyps discovered using screening CTC?

Question 4, based on the following discussion questions, how confident are you that the

evidence demonstrates that screening CTC results in a net health benefit for Medicare beneficiaries similar

to optical colonoscopy?

Please note here, net health benefits includes the decrease in morbidity and mortality from the identification and removal of polyps balanced with the risks of the procedure and the identification of extra-colonic abnormalities. It does not include costs.

Voting on question 4, please note that the panel will consider discussion question A through B as follows:

Question A, does the health benefit depend upon polyp size, referral for colonoscopy, and/or interval before subsequent screening? If your answer is yes, what does the evidence demonstrate to be the appropriate recommendations for these factors?

Please note here that all identified polyps are typically removed during optical colonoscopy regardless of their size. Guidelines for CTC screening must determine whether to refer all polyps

or only those of certain sizes.

Discussion question B, does the health

benefit depend on the scanner resolution? If your answer is yes, what does the evidence demonstrate to be the lowest resolution that should be used?

Question C, does the health benefit depend upon the skills of the individual performing and interpreting the screening CTC? If so, what should be the minimal training and experience for those individuals?

Discussion question D, how should extra-colonic findings of CTC screening be reported and treated?

Voting question 6, how confident are you that the evidence demonstrates that the use of CTC screening in the average risk Medicare population will increase overall colorectal cancer screening in that population?

Voting question 7, how confident are you that there is sufficient evidence to determine the appropriate CTC guidelines for referral for polyp

20 removal and for frequency of screening?

21 Finally, discussion question A, how can

adherence to CTC guidelines and compliance with referrals for optical colonoscopy be monitored and maximized?

That completes my presentation. Unless you have questions, I will turn it over to Mary Barton for her presentation. Thank you very much.

DR. MC NEIL: Thank you, Mary. Thank you, Bill.

DR. BARTON: Thank you very much. I am here presenting the work of my colleague, Eva Whitlock, and her team at the Oregon Health Sciences and Oregon EPC. All the credit for what I am about to say goes to them for the work that's been done synthesizing evidence. Any demerits in the presentation are mine alone. And if I slip into the first person while I'm speaking, please forgive me. Thanks to the U.S. Preventive Services Task Force members who volunteered their time as well as the expert consultants and peer reviewers.

This talk is to summarize part of the

information prepared for the U.S. Preventive Services Task Force by the Oregon EPC. And it focuses on the

efficacy and harms, as well as uncertainties remaining regarding CT colonography for primary colorectal screening.

The last time the U.S. Preventive Services Task Force made a recommendation on colorectal cancer screening, it included a strong general statement that adults age 50 and older should be screened with one of the listed options. If you look at the text of that recommendation list or statement that the Task Force found at that time insufficient evidence to be able to recommend for or against CT colonography.

The big picture here is that the Task Force uses an analytic framework when working on a systematic review of a topic. And the big question is sort of to look for direct evidence of health impact. When that's not available, then they look to bodies of evidence on questions such as screening accuracy, harms, et cetera.

The focus of today's presentation includes

this part of the analytic framework. The efficacy of newer screening technologies for colorectal cancer

detection which, for this full review done by the Oregon EPC, included high sensitivity FOBT, fecal immunochemical tests, fecal DNA, and CT colonography. Also, I just note question three, the harms of each of these screening modalities.

The methods used for the systematic evidence review are clearly laid out in both the publication of the Annals of Internal Medicine as well as on a longer technical report that's posted on ARC's (phonetic) website. But if you want to ask me later about the acronyms here, I can tell you what those refer to.

But I think it's important here to note that the systematic evidence review focused on data from screening populations, so the application of tests in average risk asymptomatic patients age 50 and older. The numbers below that included studies -- I'll just note, that for efficacy, harms, and extra-colonic findings, most studies of CTC are not mutually exclusive. Several studies contributed evidence in

multiple categories.

The systematic reviewers found two good

quality systematic reviews or meta-analyses of CTC since the last time the Task Force had updated this topic. Mulhall, in 2005, summarized 33 studies and found that for small polyps, those between six and nine millimeters, there was variable sensitivity of CTC with a range of 30 to 95 percent.

A meta-regression of those 33 studies showed a higher sensitivity which was found with smaller CTC slice thickness or collimation with multi-detector CT and with two-dimensional plus three-dimensional or three-D fly-through imaging only.

For the purposes of the Task Force's consideration, it's noted that only four of the thirty-three studies were in average risk populations for screening purposes.

Second, Hayes study is a proprietary database review which updated the Mulhall search and found no additional studies identified through December of '05.

So because of the questionable applicability

of screening tests in persons who are undergoing

surveillance for a known disease, the EPC limited their inclusion of studies to those that had surveillance populations less than 50 percent. Furthermore, patients who had symptoms, patients with iron deficiency, anemia, or people with positive FOBT were not considered to be acceptable populations for extrapolation of test accuracy studies. Therefore, they limited inclusion of studies in those populations to smaller than ten percent of the total study population.

Further, we required studies to use colonoscopy as the reference standard, to have the full spectrum of disease represented in the participants. That is, they cannot examine with colonoscopy only those known to have colorectal and those known to be disease-free and not to exclude participants with indeterminate test results. Case control studies were excluded as the study has been shown to exaggerate sensitivity.

Seven studies of CTC screening were located with an N of 4,468 patients. Three of the studies

were eliminated because of single-detector CT technology, not reporting per patient sensitivity and specificity, or quality concerns. The removal of those three resulted in four fair or good quality relevant studies that are discussed, which fortunately include over 4300 patients. So there's not a large loss of N from those three studies for quality reasons.

This table shows the data from the CTC trials with the optical colonoscopy data from Pickhardt for comparison purposes in the first column. Sensitivity is shown for cancer and for adenomas of ten millimeters and larger or six millimeters and larger.

Pickhardt for the CTC column performs CTC using six radiologists. Optical colonoscopy was performed by seventeen colonoscopists. The fecal tagging and three-D endoluminal technique, in that study, sensitivity was -- for cancers and for polyps

indistinguishable from optical colonoscopy.

Next, the ACRIN study, larger, was done at

15 sites. They used certified -- a certified process to include radiologists that 500 cases have been read and that either a training course -- or that a training course was attended and that all radiologists had to pass an examination.

The technology used for that study used fecal tagging, two-D and three-D with collimation of .6 to 1.25 millimeters. It was then blinded, a full colonoscopy done same day by experienced staff gastroenterologist. But they did not use segmental un-blinding. In this study, the sensitivity is now distinguishable from optical colonoscopy for CTC, in particular, for smaller adenomas.

The last column refers to two rather small studies, Kim, which has two radiologists and five gastroenterologists, no fecal tagging and three-D virtual dissection as the technique for CTC and Johnson, three radiologists and fifty colonoscopists, no fecal tagging and three-D virtual dissection. The

ranges here are presented for Kim and Johnson as comparisons. We're comparing readers, slice

thickness, and two-D versus three-D. So they have a range of findings for the sensitivity of CTC.

I want to note that here at the bottom that referral to colonoscopy reflects the impact of the CTC screening, the threshold used for referral to colonoscopy upon detection of a polyp of a given size. And the reason why there are two numbers here for the ACRIN study is that they actually report two different numbers in their paper.

So if we're using a five millimeter cutoff, one in six people would be referred to colonoscopy. If using a six millimeter cutoff, one in eight people would be referred ultimately to colonoscopy.

The two largest studies of CTC cover 87 percent of all patients studied. We found that a sensitivity for larger adenomas were comparable to colonoscopy. However, there was uncertainty for smaller adenomas and there were wide confidence intervals.

ACRIN, in particular, had incomplete follow-

up. So 15 completed out of 27 asked to have, quote,

"second look colonoscopies," which was a quality check upon review of the colonoscopy video together with the CTC to see if there was anybody who should have a second look and be called back. And they were not able to retrieve all of those patients. The range of sensitivity in ACRIN for large adenomas and colorectal cancer is sixty-seven to a hundred -- between sixty-seven and a hundred percent.

The two smaller studies, Kim '07 and Johnson '07, the results are generally consistent with better sensitivity for larger compared to smaller lesions. They found no clear differences between the two-dimensional and three-dimensional approaches. And this was -- they were confirmed by ACRIN. And they demonstrated some degree of inter-reader variability.

The effectiveness of colonoscopy here is reflecting the findings from the CTC studies. So three cross-sectional diagnostic accuracy studies of colonoscopy versus CTC after segmental un-blinding or

20 re-examination.

21 Note that the smallish numbers here at the

top, six radiologists, two radiologists, three radiologists, in contrast with their rather larger number of gastroenterologists involved in these studies has some indications for the studies' capacity, I believe, to do quality control and the degree of baseline operator variation that's likely to be seen.

So colonoscopy sensitivity for colorectal cancer varies widely. This has to be seen as due to the very small numbers of colorectal cancers in the populations studies. The sensitivity for colonoscopy for large adenomas ranged from 77 to 100 percent. Colonoscopy sensitivity for smaller polyps is harder to estimate given inconsistent reporting. But the Pickhardt study together with evidence from tandem colonoscopy studies suggests that it is likely that the miss rate is on the order of ten percent for optical colonoscopy for smaller adenomas.

There are harms of CTC colonography. And

what are the harms in contrast or in concert from

colonoscopy when it's performed in the community

practice setting? The EPC reviewed systematically selected case series and studies of screening registries, as well as trials, cohort and cross-sectional studies.

This slide combines data on risks or harms from CTC on the top of slide and procedural harms for optical colonoscopy on the bottom. We define serious complications as adverse events requiring hospital admission, including perforation, major bleeding requiring transfusion, diverticulitis, severe abdominal pain, cardiovascular events, and deaths attributable to colonoscopy. One study also included emergency department visits.

CTC data indicated very few complications. And what complications there were were concentrated in people who were being evaluated for symptoms as opposed to true screening populations.

Optical colonoscopy complications are significantly more common. Only three of the twelve

20 studies available reported a number or proportion of

21 patients who had polypectomies performed at the time

of colonoscopy, which ranged in those three studies from 41 to 68 percent. So in those three studies where this is attributable, it's shown that the majority, over 90 percent, of serious complications, perforations, or major bleeding were in colonoscopies with polypectomies.

So now we're moving into a range where we have less precise data and more uncertainty, potential harms for CT colonography. So radiation exposure is something that comes with any CT scan. The median radiation does per CT colonography for dual positioning has been found in studies to be between 8.8 and 10.2 millisieverts. That shows the full range from 1.6 to 24 millisieverts. In context, this is equivalent to approximately 147 to 170 chest X-rays.

The no-linear threshold model estimates which come from the health risks from exposure to low levels of ionizing radiation, BIER seven, phase two, report, from the National Research Council indicate

that potentially one additional individual per

thousand might develop cancer from exposure of ten

millisieverts above background. This is in the context of 420 per 1,000 who would be expected to develop cancer from other reasons. Specifically, this radiation impact is thought not to increase risks by want of lung cancers.

Another major area of uncertainty is related to extra-colonic findings. Nine studies with over 12,000 patients reported estimates of extra-colonic findings in asymptomatic persons. The definition of high clinical significance includes findings that require surgical treatment, medical intervention, or further investigation. For example, solid organ masses or chest nodules.

Moderate importance findings were defined as those that do not require medical attention, but would likely require recognition, investigation, or future treatments such as renal calculi and small adrenal masses. Of no importance are those that are thought not to require further investigation or treatment.

So in the available studies, between 7 and 16 percent of persons undergoing CTC had findings of

either high or moderate importance. And this is actually a conservative estimate. And likely the true incidence in a very large population could be even larger.

The studies that are available to us now vary in terms of the quality and the duration of their follow-up of patients who have these moderate importance findings. And at this point, none of the available data articulate the true net health benefit or net harm of finding these unrelated findings.

Other uncertainties with CT colonography, well, the referral threshold for colonoscopy, which I'm sure we're hear a lot more about today, CTC surveillance is proposed in some areas for one or two six to nine millimeter polyps.

The second point, if CT colonography is done in a setting that does not have same day access to optical colonoscopy, then it is not clear what the patient follow-up sequence is going to be or the

proportion of adherence is going to be and how the

health systems can help people be sure to follow up

when they're referred to have colonoscopy follow-up. And, of course, if you have -- schedule an optical colonoscopy on a different day, then you're talking about two different bowel preps.

And then finally, after an all clear on one CTC, what would be the call-back interval? When would be the repeat screening after a normal test, five years, ten years?

A few other uncertainties about the current practice of CT colonography, the community performance we understand is rather variable. So inter-reader variability in non-academic radiologists, a proportion of currently categorized cases ranged from 53 to 93 percent. In ACRIN, its 15 certified readers varied from 67 to 100 percent.

I'll note that the reader certification in ACRIN, I mentioned before, that there is a test. Apparently 50 percent of those taking the test failed on initial certifying exam.

In summary, test performance for direct visualization techniques, we have the comparison of

colonoscopy -- and this is data from the CTC studies -- versus CT colonography. And notable here that per patient sensitivity of the two technologies don't differ for large lesions and, in fact, overall, not for small lesions either. Sensitivity with a range that is close enough to what's understood for colonoscopy.

But for specificity of smaller lesions, it's possible that the specificity for CTC is considerably lower. And, in fact, we don't yet have a language for describing the specificity of optical colonoscopy since I've been told that that has been the reference standard.

Other technological considerations, just in summary, the reader training, low dose radiation has been mentioned before, extra-colonic findings, and then the cost. The colonoscopy also, it must be said, sensitivity varies by operator. And possibly the harms vary by operator as well.

So in conclusion, the accuracy of CTC in controlled settings is as good as optical colonoscopy

for colorectal cancer in large adenomas of ten millimeters or larger. The sensitivity of CTC for smaller adenomas, six millimeters or larger, is not clearly comparable to colonoscopy.

And then the referral threshold for colonoscopy at this time is based on expert opinion with most suggesting referral for six millimeter or greater lesions detected on CTC. Depending on the system and the operators doing CTC, this suggests that this point between one and three and one in eight patients undergoing CTC would immediately be referred to colonoscopy.

It's possible that fewer may be referred if surveillance is an approved technique. And right now, there's a study under an IRB-approved protocol at the University of Wisconsin using surveillance protocol for persons with more than two six- to nine-millimeter lesions found on CTC.

The harms from CTC are in the immediate

short-term negligible. But we don't know about the

longer term. And, in fact, what we can surmise about

the impact of the one time radiation dose does not take into account that this would potentially be a test that would be repeated over someone's lifetime.

Colonoscopy accuracy, our current accepted standard, is not 100 percent accurate either. And the harms of colonoscopy are not negligible in the least. So quality assurance is crucial for any operator-dependent technology-dependent screening test.

I would just note in conclusion that there is an NIH consensus conference scheduled for February 2010, to look at issues related to implementation and adherence for screening tests for colorectal cancer. That is a report for future research which would include spectrum evaluations of small and medium-sized adenomas, validation of the availability and performance of community CTC, and proficiency standards for CTC, validation of risk indices, and then well-designed cohort studies in representative average-risk populations to evaluate test positivity,

diagnostic yield, accuracy, and efficiency of validated risk indices.

With that, I will conclude and be happy to take questions.

DR. MC NEIL: Are there questions for Dr. Barton from the panel?

DR. GOODMAN: Thank you, Dr. Barton. On your slide that said so many test performance for direct visualization, it was about four slides ago. You made some comments about the specificity of CTC for the smaller polyps, and I didn't quite catch your message there. Under specificity, CTC, you said something about the uncertainty with regard to the smaller ones. Are you referring to the greater than six millimeters?

DR. BARTON: That's right. So in the available studies comparing CT colonography and optical colonoscopy head to head.

DR. GOODMAN: Head to head.

DR. BARTON: So either with segmental un-blinding or the subsequent colonoscopy, the

20 specificity of CTC for lesions of this size was

21 estimated in the study from the available data to be

between 80 and 88 percent.

DR. GOODMAN: Did you cull that out for a particular reason?

DR. BARTON: Well, presumably we understand colonoscopy to be a hundred percent specific. That's probably an imperfect assessment. But that is historically what -- the way that we imagine that kind of visual opportunity and also not only visual, but the physical manipulation of a colonoscope to try and find lesions and follow up on lesions and snare lesions.

So a screening test that has a specificity below 90 percent is going to refer a lot of people for further follow-up. And this is a similar question that the Preventive Services Task Force looked at with regard to SENSA which is one of the high sensitivity stool tests. It also has a relatively low specificity.

DR. GOODMAN: So you appear to find the 80

to 88 as relatively low specificity in this instance?

DR. BARTON: I am.

MR. LACEY: Following along that line, I'm not certain that colonoscopy has a hundred percent specificity. And it might be interesting to see if some of the panel members or others would contribute to that. But in the recent JAMA Legion (phonetic) paper, the reported -- the negative predictive value of CTC was close to 100 percent or 99 percent, which would suggest that it successfully does not -- successfully pulls people who do not have colon cancer and successfully screens them.

So I guess the question would be whether or not -- it looks like ten percent of people who have to go on to an additional confirmatory colonoscopy relative to the success of it as a screening tool would have to be weighed. So it doesn't -- I'm not sure where -- whether that would really be viewed as low figure relative to other screening technologies.

DR. BARTON: I'm not comfortable I've been able to hear your question accurately. So let me see

if I can -- you're asking about --

MR. LACEY: Well, first off, I'll speak up.

I'm sorry. I must not have been close enough to the microphone. In the Legion paper, they calculated the negative predictive value for CTC of close to 100 percent, 99 percent, which means that it would successfully eliminate those who do not have colon -- polyps above six.

DR. BARTON: I would have to look myself more closely at the ACRIN calculations that you're referring to because if they were including negative predictive value of a testing sequence versus just the initial test, that would strongly influence the result that they have. I will be glad to look at that more closely in the next hour and get back to you.

MR. LACEY: That would be great. The question I would have is colonoscopy, though, the result standard, I would be interested to know what both the inter-reader variability as well as, you know, what the actual specificity is. I don't know what other kind of gold standard you would use. But

it would seem that inter-reader variability would also

be a factor in colonoscopy based on previous

literature. I just can't recall the specifics of that. So it would seem to me that, you know, we shouldn't over-interpret a number of 80 to 88 percent in conjunction with the sensitivity numbers that are matching colonoscopy. So it seems equivalent.

DR. BARTON: I would just mention that I know the gastroenterology community is working on -- it's understood that there's a lot -- there is observer variation for optical colonoscopy, and there is sufficient data in the last five years, I think, to be able to say what kind of procedural aspects improve the quality of colonoscopy and that efforts of the gastroenterology community to create and adhere to standard for quality colonoscopy are to be applied.

And I would imagine that over time, any community that had a technology where there was some observable observer variation would embark upon such a process to ensure the high quality use of that technology.

DR. MC NEIL: Mary, while this slide is up, we were discussing this this morning. Under

sensitivity greater than or equal to six millimeters, that includes six, seven, eight, nine, ten and eleven, twelve, thirteen. Right? Greater or equal to ten is ten, eleven, twelve, thirteen. So that means greater than or equal to six includes greater than or equal to ten.

DR. BARTON: (Nodding head.)

DR. MC NEIL: So how is it that the sensitivity is less?

DR. BARTON: Well, if the numerator and denominator of --

DR. MC NEIL: The adenomas are the adenomas. They are what they are. That's the true comparing of the colonoscopy. So it's just the number found that varied?

DR. BARTON: Right. It's the number of polyps ten millimeters and greater with adenomas. Ten millimeters and greater is smaller than the total number of six millimeters and greater.

DR. MC NEIL: So the number -- so that sensitivity applies only to adenomas -- I'm trying to

understand what the denominators in both of those are.

DR. BARTON: I think I understand your question. So if the denominator for the sensitivity calculation is only those adenomas greater than ten millimeters, and the denominator for this is a larger number because it includes all of that denominator plus it adds more, and the test potentially has some detriment in accuracy as you're starting to look at smaller lesions, then you would have a smaller overall ratio.

DR. MC NEIL: But you don't have any data from just six to ten.

DR. BARTON: No. That was -- the limitations of the available studies in terms of how they reported things out does limit us to this kind of --

DR. MOCK: I just had a couple questions regarding the harms along the lines of this being a screening test evaluation. In particular this slide

refers to 28 per 10,000 serious harms by colonoscopy.

And there's a slide later in the presentation that

refers to conclusions, CTC harms that states that the estimate is 1 cancer per 1,000 screening CTC.

So I had some questions regarding that information. First, what age population were these drawn from? Are we talking about the Medicare age population or the overall population?

And secondly, this estimate of 1 per 1,000 harmed by radiation-causing cancer, is that only for the screening, or is that for each inclusive CTC examination?

DR. BARTON: So to take the second question first, the -- really the no threshold model which is derived from historical data about radiation impact has a best estimate which, I've said, one per thousand for a ten millisievert exposure. But the confidence intervals around that are very wide. The historical data is thankfully not super rich to enable us to understand the health impacts of radiation. But it is clear from -- nobody would seek extra radiation

unless they had a reason to.

But we don't -- but I would have to say that

the confidence intervals are very wide around that estimate of one in a thousand.

UNKNOWN MALE VOICE: Okay. Now to get to the question about age yet. So if there's 28 per 10,000 harms in a colonoscopy experience, then does that mean that there's 30 per 1,000 cancers caused by screening CTC?

DR. BARTON: I'm not sure that I follow --

UNKNOWN MALE VOICE: If it's per 1,000 then versus 28 per 10,000, is that 30 per 10,000 for cancers caused by CTC?

DR. BARTON: The harms from colonoscopy are procedural harms related to anesthesia and manipulation of the colon. And I would say just also to remember that the harms of colonoscopy are risked by everyone who undergoes a colonoscopy, whether for screening or diagnostic purposes.

And that the nature of any screening test, whether it's a stool-based test or CTC that functions

to sort people into getting colonoscopy or not, will

be -- it's efficiency will be maximally -- you know,

the maximal accuracy will happen when it sorts people correctly and sends a few people to risky colonoscopy as possible.

UNKNOWN MALE VOICE: Okay. And just -- I'm sorry. I didn't give you a chance to answer the question about the age population for the estimate on the cancer caused by the CTC screening.

DR. BARTON: There's not a -- that is not specific to the Medicare population estimate.

DR. SINGH: Regarding the colonoscopy and the serious harms of colonoscopy, you're right, there is not very good data and was not very good data up until recently. We have a paper in press at (unintelligible) on about 300,000 colonoscopies. And our rates of perforation are somewhere around the tune of about 65 person 100,000 colonoscopies.

And since you asked about the age, in the ages 65 and over, we had 160,000 colonoscopies, and the rates of perforation there vary from 85 per

100,000 to about 120 per 100,000 depending on how old you are. So in patients over the age of 80, the rate

is at about 120 per 100,000.

So that just gives you an idea. That's per 100,000, not per 10,000.

DR. MC NEIL: Could you repeat those numbers?

DR. SINGH: Yes. So again, the rates vary a lot between whether it's a screening population or whether it's not. Screening populations rates are about half of these.

DR. MC NEIL: So for the screening population for individuals over 65, could you just say again what you -- I didn't quite catch those numbers.

DR. SINGH: For the screening population of individuals over age 65, their rates would be around -- again, I don't have the data right here, but I can find it for you. It would be around 65 to 90 per 100,000 colonoscopies.

DR. MC NEIL: And those are perforations?

DR. SINGH: Those are perforations, yes,

which is the most important complication of the colonoscopy.

DR. MC NEIL: So wait a minute. We have Steve Teutsch, Steve Pearson, and then Jed.

DR. SINGH: (Unintelligible.) That's the other thing I wanted to find out.

DR. TEUTSCH: Thank you for that. I wonder if you could elaborate a little bit more on the extra-colonic findings and any estimates of how -- because they're very common and obviously, not terribly well characterized. But if you could talk about how you would bound the limits of the potential harms or the potential benefits?

I mean, I understand that there was no conclusion. But since they're very common, it seems like there's a potential that they would outweigh any potential benefit of the colon cancer detection. So can you bound the limits of the potential benefits and harms for us in such a way that we can get a better handle on the uncertainty?

DR. BARTON: Well, that's an excellent

question, and I would say that the bounds on the

upside, we would have to look at possibly from whole

body CT scans which have looked at, you know, the asymptomatic detection of a variety of lesions. And while there may be cases in which there's a fortunate detection of a lesion that can be managed differently because it's found early, in fact, we don't have good data from those kind of sequences to suggest a major population benefit.

And on the harm side, all I can say is that when someone comes into my office seeking screening, they feel good. And they're not -- they're not coming to me with a problem. So anything that I do to them that increases the risk of someone putting a needle in them, I would take extremely seriously as a primary-care clinician.

So I think that the down side of running after, say, 15 to 20 percent of people who have a CTC to track down one lesion or another has to be considered potentially consuming an awful lot of patient time, not to mention the resources of the

health care system, not to mention the anxiety and concern of the patients undergoing that evaluation.

DR. MC NEIL: Steve, Jed, and then Bob.

DR. PEARSON: I'm sure we'll hear a lot about incidental findings in terms of the profession's attempts to create guidelines on how they should be managed. A lot of them are going to be the standard, follow-up in three months with another scan perhaps, as opposed to a needle.

But I just wanted to clarify one thing and then two quick questions. It seems that even though the questions that we've been asked have to do with 16 slice and greater, I take it from the evidence review, the only articles that have been talked about so far are 64 slice or greater. I just want to confirm that from your perspective.

DR. BARTON: That is my thought, but I will double check.

DR. PEARSON: Okay. I'm pretty sure that the weight of the evidence that you've talked about, if not all of it, is from 64 slice or greater.

Two things that didn't come into the purview of this evidence review, but I just wondered if maybe

it had been, but just hadn't been summarized for us. We've talked a lot about test performance, and it's always appropriate to think about what the gold standard is. But there's also -- there's obviously a portfolio of improved methods of screening for colorectal cancer. Do you have the sensitivity and specificity of FOBT, of flex sig, and the other options that are currently covered in order for us to get some parameters for how CTC may compare with those?

And the second part I'll go ahead and ask now is, no evidence was presented on other patient relevant outcomes which might include anesthesia related harms from colonoscopy or time spent during the day. I mean, you know, you can consider this of patient relevance at least. Did any evidence review go on around those aspects of patient related outcomes?

So I kind of have two questions, one about

sensitivity and specificity versus other methods and other patient outcomes.

DR. BARTON: So the complications -- to take the second one first, the complications of colonoscopy explicitly include complications of anesthesia. So a complication of the colonoscopy includes the range of things that result from that procedure, including prep, anesthesia, and the actual manipulation of the colon.

And I would just -- that reminds me just to say that perforation is extremely important as a complication. There is some evidence in the Medicare population that hospitalizations, heart attacks, kind of other major sequelae are much more important in the elderly population than they are in the younger population.

Then back on to the other tests, so the evidence review and the article that's in the Annals of Internal Medicine covers all of those technologies. And I think I might have a slide that shows the flexible sigmoidoscopy data. So this is only one

other technique.

But in the top row here, you see flexible

sigmoidoscopy with biopsy versus flexible sigmoidoscopy without biopsy. And we have sensitivities for colorectal cancer in the 75 percent range for the without biopsy, the 58 to 62 percent for with biopsy, and for advanced neoplasia which is a definition of adenomas -- and I would have to double check the size of, you know, a lower sensitivity.

DR. PEARSON: Okay. And just to clarify, those are sensitivities for cancer. And you would assume that the sensitivity for polyps would actually be vastly lower than that. Is that correct?

DR. BARTON: Not -- not exactly. So one of the things about flexible sigmoidoscopy is that you're only visualizing a part of the colon. And because your next test is a colonoscopy which looks at the whole colon, it's possible for something -- for a red herring in the distal colon to then buy you a colonoscopy which finds something proximal.

And so that the sensitivity of --

sensitivity for flexible sigmoidoscopy is a little --

little different than some of the -- than looking at,

for example, CTC versus optical colonoscopy. So I can't say exactly right off that the sensitivity is lower for polyps of a particular size, although it's possible.

DR. MC NEIL: Let's see. Jed and then Bob.

DR. WEISSBERG: Thank you, Barbara. Just wanted to comment a little bit more on the harms of optical colonoscopy and perforations. The population-based studies that you mentioned are as they are.

But it's interesting that if you look at surgical papers looking at complications of colonoscopy and repair techniques, you know, not a population-based, but a referral-based kind of study, it's not the case that most of them report prior polypectomy. It's actually much more mechanical torque injuries to the sigmoid colon. And we should just note that the -- not only the accuracy and completion rate of a colonoscopy differs by operator, but the complications rates may very well as well.

DR. MORRIS: I'd like to just say a word about that last comment. And that is that if a

perforation occurs because of a polypectomy, that can often be solved without an operation whereas a torquing or a shear injury needs to be operated on.

DR. MC NEIL: Let's see. It was Dr. McDonough. Bob, did you have a --

DR. MC DONOUGH: Yes. This is a question I don't know if you know the answer to. But it's just a follow-up on that question of incidental findings. I mean, there are recommendations for screening for abdominal aortic aneurysms. If you have a normal CTC and there's no evidence on that CTC of an abdominal aortic aneurysm, would that be as good as an ultrasound examination which is usually used?

I don't know if you know the answer to that. In other words, can you get two screenings for one?

DR. BARTON: Well, I do know that one of the issues related to a potential question about extra-colonic findings is that if CTCs are done without the same kind of contrast that body CTs would be done

with, then, in fact, I think you can't expect

radiologists to be able to detect all the lesions.

But I would actually defer perhaps to your chair to answer that.

DR. MC NEIL: Not to me on that one. Let's see. Yes?

DR. PEDEN: I'm just wondering if there's any information from the studies that you reviewed about the ability to actually complete a test and the comparison between CTC and optical colonography and whether that varies by age.

DR. BARTON: That's an excellent question, and I am pretty sure that the experience, the published experience with CTC is all in trial situations. And so even if there was a report of issues related to completion, adequacy of prep, I would think it would be unfair to assume that that would be true for the general population. So I think CTC is probably too early to have a good estimate for that yet.

For optical colonoscopy completion and

whether it varies by age, I don't believe that that

was information that we found in this report. But I

have a feeling that it must be reported on. And I can try to find that as well.

DR. MC NEIL: Could I follow that up with one question, Mary? And you probably don't know the answer because it's similar to this other question. Are there data on the percentage of Medicare patients who would be unable to participate in the screening CT for some other reason, just not participate at all?

I'm sorry. They wouldn't be able to participate in the colonoscopy, but could participate in the CT colonography perhaps by reason of being high anesthesia risks or whatever. I don't know what the whatever else is.

DR. BARTON: I don't know that there's data yet about that. But I -- but my thought here is that colorectal cancer screening is very important for the general population. But adenomas take a good long time to turn into cancer. And for this reason, the Preventive Services Task Force has recommended that

nobody over 85 should be screened, and that you should

think hard between -- about screening people between

the ages of 75 and 85.

And so for some slice of the population that's too frail to undergo colonoscopy, you wonder if they should be screened for colorectal cancer at all. But I think I'm -- it's certainly theoretically possible that there are people who are unable, even for a temporary reason or an enduring reason, to join in an optical colonoscopy program.

DR. MC NEIL: Dr. Morris, do you have any comments on that?

DR. MORRIS: I'm sorry?

DR. MC NEIL: Do you have any comments on whether or not there would be a factor of the Medical population that should be screened, that is between, say, 65 and 78 -- pick some number -- who couldn't do colonoscopy because they were high risk patients for anesthesia or some other reason and hence, for whom colonography would be good?

DR. MORRIS: Yes. Actually, I was thinking

about a couple of my patients just as you were saying that. And these are people that we would not want to

sedate unless we had to put them under with intubation.

DR. MC NEIL: Why wouldn't you want to sedate them?

DR. MORRIS: Because of potential dementia or some sort of pulmonary compromise, primarily dementia and concerns about potential aspiration or inability to guard the airway.

DR. MC NEIL: Dr. Weiner?

DR. WEINER: Perhaps Dr. Barton, you found something in the literature on behavioral aspects, patient perceptions, or perhaps some of the other presenters will address it. You know, one of the arguments, of course, is greater uptake rates because people will get CTC and won't get optical colonoscopy. Any comment on that, or should we reserve that question for later?

DR. BARTON: Issues of adherence were expressly excluded from the systematic evidence review

prepared by Oregon at the request of the Preventive Services Task Force. So that is not included in this

literature review.

DR. WEINER: Okay. Thank you.

DR. MOCK: I just note, though, along those lines that the ACRIN study was voted as only fair quality because the lack of follow-up. Is that -- was that due to adherence? Is that what that was referring to?

DR. BARTON: No. I think I understood the question about adherence was more along the lines of your doctor tells you to get screened, and then you never follow-up. So the very front end adherence question. The ACRIN study fair quality assessment -- I think that the follow-up -- yes. So the sequence by which they double checked the CTC findings and the colonoscopy findings was incomplete.

DR. SINGH: Could you explain that a little bit more?

DR. BARTON: Explain the second look colonoscopy?

DR. SINGH: No. This last statement that you made that the way they followed up was incomplete.

DR. BARTON: So the Pickhardt study and some other studies of optical colonoscopy compared to CTC have used a technique called segmental un-blinding, which provides really a new standard in a way to think about reviewing the colon whereby they sort of gave sequential slices of the CTC reading to the colonoscopist.

And they basically, you know, had the colonoscopist doing a segment without knowing what the CTC showed, saying what he or she found, and then being told -- revealed what the CTC had found so that they could then go back over that very segment to see if they had missed -- you know, to look again in places where the CTC had been abnormal, for example.

So that segmental un-blinding standard is likely to yield the answer closest to the truth of what's in the colon. And the ACRIN study didn't use the segmental un-blinding approach. They had an experienced colonoscopist do a colonoscopy. But they

did not have the CTC results.

And so they created this second look

sequence to say, you know, for people who had something on CTC in our database, but an optical colonoscopy reading that was normal. Well, let's go and look at the video of the optical colonoscopy and the reading of the CTC and look at them together. And if we think there's something that merits getting the patient back in here, we'll ask them to come back.

Well, only half of them came back. So we have an incomplete ascertainment basically.

DR. MC NEIL: I'm sorry. One final question.

DR. MORRIS: Particularly with a practical application that this would not really be an issue because we would certainly want for our colonoscopists to know the result of the CTC that happened beforehand?

DR. BARTON: It wouldn't be blind.

DR. SINGH: No. Actually, she's trying to comment on the quality of the data from the study

because if you're comparing sensitivity and

specificity versus say, a gold standard of the

(unintelligible), then perhaps a better way to do it is with the segmental un-blinding that she's talking about.

But you're right for practical terms. But I don't think that's what Dr. Barton was referring to. She's referring to why the study was called fair rather than excellent.

DR. MORRIS: So it sounds to me like in the practical world, that potentially the sensitivity would actually be better than in a study.

DR. BARTON: Except for in the practical world, you would be using CTC to sort some people to never get a colonoscopy.

DR. SINGH: Exactly.

DR. BARTON: So they would never have that. Well, it's true that the people who were sorted into getting a colonoscopy would have both test results available to them. Any -- any previous screening test, whether it's FOBT or CTC, you're basically

sorting the population into a whole -- you know, a set

that don't need optical colonoscopy.

DR. MORRIS: We're talking about the sensitivity of the CTC. Aren't we?

DR. SINGH: Right.

DR. MORRIS: So would the sensitivity be better if the follow-up colonoscopy -- oh, I suppose -- yeah. I get what you're saying. Okay.

DR. MC NEIL: You know, at this point, I think we should go on and hear what the U.S. Preventive Services Task Force said. Are you going to be able to stay around for a bit, Dr. Barton?

DR. BARTON: I shall.

DR. MC NEIL: So why don't we hear what they have to say. And then if there's some joint questions from both -- for both of you, we could take them at that time. So thank you very much.

So Dr. Calonge from the U.S. Preventive Services Task Force.

DR. CALONGE: Good morning. I'm pleased to be here, and I wanted to personally thank the

Committee members for the work that you do on behalf of CMS and my tax dollars at work.

Just to remind folks, the U.S. Preventive Services Task Force is an independent 16-member panel of nationally recognized non-federal experts experienced in a variety of areas, including primary care, prevention, evidence-based medicine, and research methods.

And we are charged by the Congress to review scientific evidence for clinical preventive services and develop evidence recommendations for the health care community. We base our recommendations on systematic evidence reviews by AHRQ's evidence-based practice centers. And you've just experienced a presentation of one of those reviews.

So in making a recommendation, what do we consider? What are the nuts and bolts of how we turn what you just heard from Dr. Barton and the Oregon EPC into real recommendations?

So where we first look is, are there overarching evidence of net benefit of randomized

control screening trials? And I hope everyone

recognizes that for -- once we get beyond FOBT,

everything is indirect evidence because we don't have screening trials that are looking at visualization or CT colonography.

However, we get to number two, is there evidence that screening leads to improvements in important health outcomes along a chain of evidence in terms of benefits? And so tying visualization, either by radiographic techniques or direct visualization, to health benefits is possible along a chain of evidence. So we can assign potential important health benefits. But then we look at, are there evidences that screening leads to important harms?

I wanted to hit the last point. Dr. Teutsch actually talked about it. In lieu of good evidence of harms which we often suffer from in our methods, can we look at the potential harms, and can we estimate those or at least try to bound or figure out what the higher end is? And can we qualify that higher end as

no more than small?

So in other words, we want to be able to

compare benefits as being, you know, small, moderate, or large and harms as being at least small, if we can, if we don't have good evidence.

So when we looked at the CTC evidence that you just looked, we concluded that sensitivity of CT colonography for cancers and large adenomas probably is comparable to optical colonoscopy.

And I wanted to actually answer a question from the end of the table. Sensitivity is what drives positive predicted value. Specificity drives negative predicted value. And so -- I'm sorry -- positive predicted value. So the real concern on the low specificity is that you refer more people for optical colonoscopies. So it's a fascinating area of screening in that the benefits, the important health benefits, are tied with how many colonoscopies you do, and the important harms are tied to how many colonoscopies you do.

So the purpose of CT colonography is to try

to do less colonoscopies, but do the right non-

colonoscopies, you know, exclude the right ones. And

so to the degree that we do more colonoscopies, CTC as part of a screening sequence is less valuable. So I hope that helps.

So we looked at that. We said the sensitivity was good, so, therefore, the negative predicted value would be expected to be good. Number two, the immediate harms of CTC are low compared to colonoscopy. And I heard some debate among members already that we may have set our harms for colonography -- sorry -- colonoscopy a little bit high. But I think those are things that you'll have to weigh.

But then there are important unknowns. What's the impact of the relatively high dose of CT radiation, especially over a lifetime with repeated screens? So the question about it would be one in a thousand additional cancers associated with each CT colonography at the ten millisieverts level.

And then final clinical results and health

system impact of the extra-colonic factors were things

that we looked at with the important unknowns.

So I think we talked about this already. The radiation for a single administration would be in the no threshold linear model, which is a model with some controversy around it. But looking at that, we see estimates of one in a thousand undergoing a single CTC could develop cancer from the exposure.

And the extra-colonic findings, 7 to 16 percent of tests, depending on the study, resulted in additional diagnostic workup suggested. So we looked at this issue of potential harms as being potentially not small.

So in our process, we determined the magnitude and certainty of net benefit. And we estimate the magnitude of benefit and the magnitude of harm, estimate net benefit, which is benefits minus harms, and then put a judgement of certainty by applying a certain set of critical appraisal questions. And I didn't want to spend time going through those, but I knew someone might say what are

the questions, so they're included here for reference.

And then this concept of certainty is again

a process issue I didn't want to spend much time on other than to talk about low certainty. And low certainty evidence is insufficient to assess effects on health outcomes. Additional information from future studies may allow for assessment. So this is the area of uncertainty that leads to our recommendation grid.

So what we do is we judge the evidence of benefit, the evidence of harms, we weigh those two, and we apply the certainty grid. And the way you get to a positive recommendation is you need at least moderate certainty of at least moderate benefit. And that will get you into the A or B range where we recommend use.

The C ranges are recommend against routine use, the D's are recommend against use which is a real recommendation. It's not we don't know, it's a don't do. But then you see when you get down to this issue low certainty of net benefit, we make no

recommendation. We simply conclude that the evidence is insufficient.

So for CTC, the Task Force was unable to estimate the magnitude of harms. And the potential harms could be large. And so that's the real crux of our uncertainty, that following extra-colonic findings could result in potential net harms that were not small. That is, surgery, for example, for the over-diagnosis of incidental, non-important lesions. So those could be large, as well as induction of additional solid organ tumors from excess radiation.

So because we couldn't estimate the net benefit, we gave CTC a I for insufficient evidence. Now, here's the process issue. It's important to point out that an I letter grade is a conclusion, not a recommendation, and it's really a call for more research.

There are multiple reasons for giving an I, like lack of evidence on clinical outcomes including harms, and that's where we came down having problems with CTC. So there's a possibility of clinically

important benefits. So recognize I's don't say it's

bad. So in other words, CTC could help reduce

colorectal cancer mortality. It could reduce it in the context of do we reduce mortality from screening, by not doing as many colonoscopies, or do we actually get more people to screen -- to be screened because CTC is more acceptable?

So I hope you understand that I is not evidence of no benefit. It's no evidence of net benefit. And that's kind of where we're stuck. So recognize, it's a don't do -- it's not don't do, it's not do, it's don't know.

So we're one of several bodies internationally that have looked at CT colonography in particular. And I'll just point out, I think this is the summary that we've put together, that the U.S. Multi-Society Task Force in 2008 recommended for it. Asia Pacific said don't do it, for interestingly, different reasons than the Task Force.

Institute for Clinical Systems Improvement said yes. And then the Comprehensive Cancer Network,

20 World Gastroenterology Organization, Kaiser Permanente

21 Care Management Institute, which is updating, NHS-UK

screening program, also under review, and Canada in Ontario all recommended against CTC.

DR. WEISSBERG: Ned, can I just update that from KP? The new technology committee in its last assessment did find it medically appropriate.

DR. CALONGE: Well, I appreciate that. So I'll need to change the slide.

DR. SAMSON: I also wanted to point out that the Blue Cross and Blue Shield Association also found that it met our criteria.

DR. CALONGE: Which I don't think was on our slide, so --

DR. PEARSON: And that the Institute for Clinical and Economic Review found it comparable to optical colonoscopy.

DR. CALONGE: So given that this slide could have -- one check is going to move over, and then we'd add more lines that might be in the yes column, you have to say, well, why would we look at the same data

and have conflicting recommendations?

And I think the real issue here is we often

don't have complete consideration of possible harms. And getting back to the Task Force's approach and what Mary said, you know, it's hard to approve on asymptomatic. And when we intervene in people who are asymptomatic, I think that's where we want to have the best evidence of benefits and harms. And in the fact of uncertainty, the Task Force concludes that it's uncertain.

So that gets to this last point, what's our approach to uncertainty? The trade-off between the risk of being wrong and adopting the service before its benefit is proven or waiting until research proves the benefit of service when it could help people now. There's always this tension around the I's that we have to face in both clinical medicine and as a recommending body.

So again, if I was going to summarize the Task Force findings is that we believe we found that CTC, at least for a ten millimeter and larger polyps,

was comparable in terms of testing performance to colonoscopy. And so that was on the benefits side.

So I would say we would expect the benefits of screening with CTC to be similar to those on the colonoscopy-only based program.

And then on the harms side, we were unable to confidently assign an upper bound to the harms. We concluded that it's at least possible that they're large. And given the inability to trade-off the benefits with the harms, we concluded with an I statement.

And with that, I'd be happy to answer questions.

DR. PHURROUGH: Let me make just a quick comment that I meant to make earlier about USPSTF's role in coverage decisions around prevention. That role changed this summer.

As many of you may be aware, until this summer, Congress had not provided a screening preventive benefit, a broad screening preventive benefit to the Medicare population. Individual

screening or prevention services were provided in separate statutes. So we have colorectal cancer

screening because in a particular law, seven years ago, six years ago, Congress says, pay for colorectal cancer screening, and here are the ones you pay for, and here's how you decide on others. We have a mammography screening benefit. We have prostate screening benefit, and there are several others.

This summer, in the Medicare Improvement whatever act, MIPA, Congress says that you may cover additional preventive services as they meet certain standards. And one of those standards is that they must have at least a B recommendation from USPSTF.

So Congress has now spoken to say, Medicare, if you're going to cover preventive services in the future, pay attention to what USPSTF has to say. We tend to pay attention to what Congress tells us. We pay a lot of attention to what Congress tells us.

And so a question we have now around those preventive services -- around those older preventive services, pre-MIPA, where we have the ability to

20 modify the scope of that particular benefit, should we

21 in fact use the same standards that Congress outlined

in MIPA, since that seems to be what Congress would like us to do in the future.

So we think it's important to pay attention to USPSTF in this particular issue, even though the law for this particular issue, colorectal cancer screening, did not require USPSTF.

DR. MC NEIL: So could I just ask one question? Should we all leave now?

DR. PHURROUGH: Well, we could. But, no. Our decision will not be wholly based upon what USPSTF has to say. But we think Congress provided some importance to that.

DR. MC NEIL: Yes. I understand. And usually when they speak, you listen. So I think we understand. Could I just ask one question? And then I'll open it to the panel.

Could I ask one question? That was a wonderful presentation, and thank you. What kind of data do you think would you want, and would it be

feasible to collect on a sample size adequate enough

to convince the skeptics in this room that would get

you out of the I category? Because the harms don't --

DR. CALONGE: You know, distinguished panels only ask excellent questions.

DR. MC NEIL: Well, it's obviously excellent.

DR. CALONGE: The issues around no linear threshold modeling, it just raises -- it will raise uncertainty --

DR. MC NEIL: Well, we'll never answer that one.

DR. CALONGE: So that's an issue that -- oh, good. So you're getting me off the hook for that one.

DR. MC NEIL: I'm in radiology. That one we'll never answer.

DR. CALONGE: On the standpoint of harms, I mean, what we really need is a study that looks at this broad-based body scanning from an ionizing radiation standpoint and says, you know, can we confidently assign risks or come up with guidelines

for looking at extra- -- I'm sorry -- incidental

lesions on full body scans, for example, so that we

know that if we only intervene in these lesions of high importance that most of the time we're finding something that we're altering the course of.

Remember, whenever you do a screening test, right, there are five things that can happen, and four of them are bad. False positive, false negatives, over-diagnosis, and you made no difference, but you used resources.

So that's the real problem, I think, with the extra-colonic findings are that how often are we actually intervening in a lesion and changing the natural history of what that condition was, and how often are we actually providing the patient with a procedure, another scan, more radiation, or other interventions that are not going to give them a positive health impact.

I would hold that everything you do to a patient that has potential harm and has no potential health benefit is something we should try to not do.

So I think a study that actually looks at the way we

approach what we see outside the colon when we do CT

colonography and follows that and sees, on the whole, did we help or harm people is what the Task Force would need to fill in that gap.

DR. MC NEIL: So can I just push this just a little bit more? The ACRIN study had 2500 patients. And I believe it -- correct me -- 18 months to -- how long did it take to collect those patients? I can't remember. Mary, do you remember? It was a while. It look a while to collect those patients.

And those patients -- and that group of investigators has data on the extra-colonic findings. So the question is, can they go work up -- go back and look and see what happened to those patients, or is it necessary to meet your standards to launch another study of 2500 patients and do a much more systematic review in which case we're talking about -- make up the numbers -- two-and-a-half years or three years -- which I think is probably what it took from start to finish for that study -- for the Preventive Services

Task Force to move off I in whatever direction.

That's really my question.

DR. CALONGE: So the answer is maybe. So the issue comes down to, can they actually find all those patients for which there were extra-colonic findings. If people are lost to follow-up, are they lost to follow-up because they survived, got out of the health care system and had no further interventions, or are they lost to follow-up because they died of the lesion that they could have benefitted from early detection.

And so it's a maybe. I would say that having information on follow-up for the extra-colonic findings from ACRIN would be helpful to the Task Force. But we would then have to apply those kind of six critical appraisal questions and come up with a level of certainty that we are at least moderately certain that there was more good than harm or that the harms we could bound to say the benefits from avoiding those colonoscopies in those patients outweigh any harms associated with the extra-colonic findings.

DR. MC NEIL: Well, maybe we can ask Dr. Johnson later today about the feasibility of that. So

Dr. Pearson?

DR. PEARSON: Thanks again. I think the USPSTF serves a tremendously important role for us all. I do quickly want to echo Barbara's question because I think even if you went back to ACRIN and you followed all the patients with incidentals, the question of lead time bias, I don't think a real kind of hard-edged clinical epidemiologist would ever be happy with the data that you can get on incidental findings. And so it kind of creates a difficult box for clinicians and developers to try to figure out how to provide adequate evidence.

I want to talk just briefly about the radiation risk, the one in a thousand, because in the evidence reviews that I've found, the only data come from estimates for 50-year-olds, lifetime risk. And they're actually one percent -- one out of a thousand is at the high end of that range.

So given that we're already -- I mean, you

20 talk about uncertainty. There's a huge uncertainty

21 around that estimate. Every estimate I've read is at

age 50. So I wonder whether you could help us understand if there's any way to extrapolate that to what we should be thinking about for the Medicare population.

DR. MC NEIL: All those estimates come from the BEIR report which related in large part to Japan. And that had a spectrum of ages.

DR. CALONGE: That's correct. And the average at age 50 is still out of the BEIR report. So you're looking at extrapolation from, you know, two extremely unfortunate events that really, thankfully, has not been repeated, nor have we really added substantially to the knowledge of the no linear threshold model.

I will tell you that being in environmental health as well as public health, the same is true of all environmental exposures. The science around environmental exposures is frustrating and young. I guess the one -- the offhand comment that I always

make is that I don't quite buy into the concept of

better living through ionizing radiation.

And I think that NIH has concluded that there is no safe level of additional ionizing radiation exposure. And, you know, I think that was based again on just not being able to find even at low levels a lower bound of increased risk.

So to get specifically to the question, the issue about the Medicare population is that, you know, they will have accrued a lot of potential tumors already. And to the degree that radiation in that age group will incite additional tumors is very uncertain in terms of applying the BEIR model.

DR. MC NEIL: Let's see. Steve, Cliff?

DR. TEUTSCH: I want to go back to the extra-colonic findings again. And I think part of the problem -- and I'll say this partly having been on the U.S. Preventive Service Task Force. One of the concerns is what one finds with a screening test is different than what one finds, of course, if one is actively looking for things because someone is

symptomatic or presents with some finding.

And so the natural history that one has for

those things is likely to be different and, therefore, simply finding them doesn't have much prediction. I think we can go back to look at what was done for low dose CT screening, CT scanning for lung cancer where we had the same set of issues and substantial uncertainty about what all of those additional nodules had and what their real natural history was.

What's the natural history of a finding that you find incidentally? It's what Steve Pearson was just referring to that. It's very difficult. And simply following people from a cohort that were screened and seeing what happens to them, without any basis for comparison, is going to be extremely hard to assess because you're going to be doing something to some of those that you suspect may progress to something of consequence. But you actually don't know.

And so that's the problem with this bounding. And it's one that the Task Force wrestles

with all the time. And you can elaborate, Ned. But it is really a problem because you see the -- because

we are screening asymptomatic people and creating potential benefits, but really you don't know what you're doing with all of these unknowns.

DR. CALONGE: I think the comment I would add, and it gets to Barbara's question and I think to Dr. Pearson's comment as well, the real benefit of looking at the ACRIN people would be if we could actually document that there was a lot of harm. That is, that people in that group died more often than the group that -- you understand what I mean? If we could more confidently assign harm. The problem with assigning non-harm is those issues.

It's going to be able to assign benefit because we don't have a control group of the benefits of extra-colonic findings or full body CT scans. So the same uncertainty that goes with full body CT scanning screening I think has to apply, except, at least, we're leaving out the head and the chest when we're doing the scanning.

DR. MC NEIL: Cliff?

DR. GOODMAN: Yes. An observation and a

question. Since you did show a slide that compared various authoritative groups' recommendations and other decision, I just wanted to observe and not make a judgement that when you look at the distribution of findings among U.S. and even global organizations that appraise evidence and make recommendations, USPSTF tends to be at the more conservative end that has perhaps one of the higher evidence thresholds compared to others.

You tend to find yourself in the company of -- Cochrane is usually pretty tough and Australia, the MSEC and the PBEC as you probably know are very tough. NICE is sometimes tough, but they're very good listeners. So sometimes -- but in any case, USPSTF tends to have a higher evidence threshold than most U.S. and global organizations. Observation, not a judgement.

Question. When you arrived at the I finding -- I just want to ask this kind of at a high level --

were you generally -- this is more for a layperson's policy-maker's viewpoint and not a practicing

physician's standpoint. Does the I level typically characterize CT colonography as largely a substitute for colonoscopy, or might it consider it as a complement?

And the reason I'm asking is that I wonder if you could envision circumstances, clinical scenarios in which they may be used as a complement. For example, CT colonography could be used as a -- excuse me -- colonoscopy could be used as the first screen in one's lifetime. And then depending upon the outcomes or the findings, CT colonography might be used later on.

And so it's not that you would get one for the rest of your life every five or ten years or the other. And I could envision some clinical scenarios where some of these dis-benefits might not flow in the way you might have considered. So as a substitute or a complement was the I?

DR. CALONGE: So the I recommendation was --

again, we looked at this. And here in the modeling

mix, again, the benefits for mortality reduction with

actually finding polyps and removing them accrue when you do more colonoscopies. Right? 'Cause you're there, and you take the lesion off.

But the problem is that the harms accrue with increasing colonoscopies as well. So we really were thinking about CTC as a precursor for deciding who -- because if you have a -- if you find something, you have to have the next procedure. So we were thinking of it in terms of kind of prioritizing people into the group that needed colonoscopies versus not.

Now, that wasn't put into the context of a one of these and three of those because that's not actually available to us in the literature where we did look to make recommendations.

What I would like to comment, though, is trying to context or shade the I, which is why you can't just leave the room. Right? It's because -- why you have to apply the questions. And even in our review in the contextual statements we said, well,

what if you couldn't -- you had the patient you

couldn't do colonography in. As long as the test is

negative, you at least accrue a great negative predictive value, and you can confidently go home and say the person doesn't have colorectal cancer now.

So I think that's on the benefit side. And the issue about adherence whether people are more likely to get screened because it's CT colonography and colonoscopy is an important question that I think you would want to wrestle with.

So I think the representative from American Cancer Society -- 'cause I've heard him say it -- would say the screening to have -- the screening to provide for colorectal cancer screening is the one the patient will get. And so if there's a role for CT colonography, is it in those patients where you can't do the test that actually allows you to do the prevention and remove the polyps at the same time? That would be the role, I think, that one could contextually look at.

Do we have research on that? No. Does that

allow us to get off the I? It doesn't allow us unless

there's evidence. So we have a I that says we can

imagine patients might be screened if they can have this and not. And that may be a benefit, and it would be a great place for additional research.

DR. MC NEIL: Okay. Let's see. One more question. Bob?

DR. MC DONOUGH: I think you kind of talked about my questions. So was there much discussion in the U.S. Preventive Services Task Force about the evidence that there are people who would opt for -- that the CTC may improve compliance?

DR. CALONGE: So again, in managing our resources on the evidence review, adherence wasn't the issue. And, in fact, looking back at Task Force recommendations, we tend not to look at adherence because the issue about the test benefit accrues to the people who actually get the test.

I think it's an excellent question. It's not something that has traditionally been within the scope of the reviews, and it's something that we talk

about in our methods all the time. Should we look more at what do people get, and should that drive the

recommendation rather than what do we know about the one statement that we really try to look at, what is our certainty of net benefit?

DR. MC NEIL: Okay. I think what we'll do is move on to our next speaker on the cost effectiveness calculations for CT colonography. And then if there's time, perhaps -- is everybody staying or is everybody leaving? Mary, are you staying? Good. Okay. Thank you.

DR. ZAUBER: Thank you very much. It's a real privilege to be here today to present this report to you. I'm discussing the cost effectiveness of CT colonography to screen for colorectal cancer. This is a report from the Cancer Intervention and Surveillance Modeling Network, which is CISNET (unintelligible). And I'm representing three independent microsimulation modeling groups, MISCAN, SimCRC, and CRC-SPIN.

And I'm delighted today to have two of my colleagues from Holland here, Marjolein van

Gallegooijen and Iris Landsdrop-Vogelaar. They're here as part of our system meeting, and we're

delighted to be here to present to the MEDCAC meeting.

The first thing I'm going to discuss is simply how do we go about using the microsimulation modeling for colorectal cancer, the methodology, the results of the discussion. Microsimulation. We all know that the adenoma is the precursor lesion for colorectal cancer. And we model this in a series of stages going from -- is there a pointer?

DR. MC NEIL: We can see it. That's all right.

DR. ZAUBER: Okay. From no lesion to an adenoma which can grow in size, then into a preclinical phase for colorectal cancer which would be part of a diagnosis, and then a clinically detectable phase, and then colorectal cancer death. At any point, the individual also could die of other causes of death.

We also know that the natural history of colorectal cancer provides an opportunity to intervene

through screening. In particular, we can intervene and find cancers at an earlier stage of disease or in

cases something like CTC or colonoscopy, we can actually detect the adenomas and remove them and also prevent colorectal cancer.

Today and in our report, we're evaluating the following strategies. For CTC, we're saying that a referral to optimal colonoscopy would occur for a six millimeter lesion or larger. And those with negative findings would have repeat CTC every five years. This is the recommendation from the American Cancer Society, the American College of Radiology, and the Multi-Society Task Force groups. So that is the strategy that we're considering for CTC.

For colonoscopy, repeat every ten years. We're looking at three of the FOBTs, Hemoccult II, Hemoccult SENSA, and fecal immunochemical tests. And that would be repeated annually. Flexible sigmoidoscopy without biopsy and with biopsy and with a repeat every five years, and sigmoidoscopy with or without the FOBT. Also we compare to no screening.

We've just talked about adherence. In order to compare the strategies comparably, we're using a

hundred percent adherence with all screening, all follow-up, and all surveillance tests. We recognize as you do that that's not what happens in practice. But we're using it as part of the modeling in order to compare across it. And we do have a sensitivity analysis on adherence.

Our cohort of interest is a previously unscreened 65-year-old U.S. population in 2005. In our report there's also tables for beginning at age 50. Our outcomes include the costs, the life-years gained, tallied from the CMS perspective, so we're modeling from payment out of CMS.

In terms of the CTC performance, we considered two base cases. Our base case analysis evaluates two sets of CTC test characteristics. And Dr. Barton has discussed these as well. The Department of Defense study, DoD we'll call it, by Perry Pickhardt published in the New England Journal, 2003, and the National CT Colonography trial, NCTC,

Dan Johnson's study, just published this year in the

New England Journal.

We consider the DoD study more likely to represent the best case for CTC in terms of the prep. We consider this to be a best case. And the NCTC trial is more likely to represent the performance in more of a community practice.

We've discussed sensitivity and specificity already this morning. I wanted to discuss it in terms of how we're modeling it. First of all, for colonoscopy and CTC, our model is using the per adenoma sensitivity. It's, of course, assumed to be that for the patient. But it's a per adenoma sensitivity.

And as you've known before, that for colonoscopy we're assuming 95 percent sensitivity for either an adenoma of size ten millimeter or larger or for colorectal cancer. And the DoD estimate is very close to that at 92 percent. The NCTC estimate is lower at 84 percent.

The what we call medium-size adenoma, six to

nine millimeters, comparability for those medium size

adenomas from the DoD study was with colonoscopy and

lower for the NCTC study at 57 percent. Colonoscopy sensitivity for the smaller adenomas, those less than six millimeters, is at 75 percent. The procedure for CTC is not to report out lesions which are less than six millimeters.

And we've also talked a lot about specificity. So let me move on over to that. We're making the assumption here that specificity for colonoscopy is ten percent. And that's because when we do colonoscopy, hyperplastic (phonetic) and other polyps are detected, and there will be some subjects who have only hyperplastic or other polyps. So we're using that ten percent to represent colonoscopies that will incur a pathology cost because of their finding of only hyperplastic polyps or other. We also just this week did a sensitivity analysis taking that up to a 20 percent false positive rate.

For the specificity for CTC is based on the specificity at the cut level of the six millimeters or

larger. So that's going to include false positives that could have included the smaller adenomas. And

for the DoD study, it was lower at 80 percent specificity, and for the NCTC we have it at 88 percent.

So I'd just like to point out that when you do CTC and with referral to colonoscopy, you are going to detect some of those smaller adenomas. There will be smaller adenomas in patients who have larger adenomas and also through the false positivity level being at six millimeters or greater, you will have some included when they go to colonoscopy.

We have costs to report and then cost-effectiveness analysis. And that's in your tables four to six in our report. And we're using for CTC the cost per screening exam, per scan, at $488 dollars. That's based on an abdomen and pelvic scan and also the processing of the scan there. And this is also -- as I said, this is CMS reimbursement cost.

For colonoscopy without a polypectomy, it's approximately $500 dollars from CMS. And colonoscopy

with polypectomy, $650 dollars. And that includes our estimate of the pathology costs where we're looking at

the number of jars per location sent to pathology. So that $650 includes the extras for polypectomy and the pathology charges. We also have charges -- costs for complications, CRC treatment by stage and phase of care.

So our analyses, our base case analyses, we're going to compare the strategies in terms of the life-years gained versus no screening. We'll then perform a cost-effectiveness analysis for CTC screening. We'll next identify a threshold cost per CTC scan such that the CTC strategy is on our efficient frontier. As a secondary analysis, we're going to address the average cost-effectiveness ratio equal to that of a ten-yearly colonoscopy screening. That was one of the questions addressed here for MEDCAC.

Furthermore, we'll do more sensitivity analysis. How does that threshold cost per CTC scan change with the screening interval, changing it from a

20 five year repeat to a ten year; the lesion size

21 triggering referral to colonoscopy, a six millimeter

versus a ten millimeter? We also, as I said, have sensitivity analysis for adherence. And then we also have the three microsimulation models independently developed using common inputs to have a comparative analysis on our results.

Incremental cost-effectiveness analysis will estimate the discounted at three percent life-years gained and lifetime costs for all the strategies. We'll order the strategies from least effective to most effective.

Then we'll eliminate strategies that are more costly and less effective than another, called dominated. We'll eliminate strategies that are most costly and less effective than a combination of other strategies, weakly dominated. And then the remaining strategies lie on the efficient frontier, where choice of strategy depends on the willingness to pay for a life-year gained.

I'm going to give just a very simply

hypothetical example. We've got nine strategies we can consider, and we're plotting the discounted life-

years gained on the Y-axis against the discounted cost on the X-axis. And we see two -- as I said, we don't have a pointer here. But you can see you've got some that have relative low life-years gained, but also lower costs. And you've got -- over on the far right, you've got something that has higher life-years gained. But it has the highest cost.

So we want to know which are the ones that essentially gave you the most life-years saved at a given level of cost. And so we're going to draw in the efficient frontier. And you see there. And you can see there are some that are quite close to the frontier.

But these strategies of consideration that for each level of cost -- and these are, you know, just hypothetical numbers. But, you know, at level, what's the value that gives you the most life-years saved?

So in particular, let's say that we're

interested in this one with the blue arrow. It's not on the efficient frontier. But what would happen,

what change in the per test or for us, per scan cost, would allow this strategy to now reach the efficient frontier? And that's when we say the threshold cost, that's the value we want to talk about. What's the value?

We're starting with $488 for CTC. And if that's not on the efficient frontier, then what would we do in terms of the cost value that would move it to the efficient frontier? Results, life-years gained versus no screening, cost-effectiveness for CTC for efficient frontier, and the threshold costs per scan.

So the first thing is, let's look at the life-years gained. And this is the results from the three models, and the red is SimCRC which we're going to use throughout. You can see it's the middle value. And for the rest of the presentation, I'll be basically focusing on that.

But you can that 171 life-years gained with colonoscopy in SimCRC, 168 with CTC using the DoD

analysis, essentially the same, a little bit less if you use the NCTC. So the first conclusion from this

analysis is indeed CTC is effective. It's a very effective strategy, almost the same life years saved as that of colonoscopy.

Now, let's go on to whether it's a cost-effectiveness strategy. So here's the actual efficient frontier. And at this point, I'm using the SimCRC model, which is the one that gave you the middle level for the life-years saved.

So what are the efficient strategies that we considered? They are Hemoccult SENSA, Hemoccult II plus sigmoidoscopy, hemoccult SENSA plus sigmoidoscopy, and colonoscopy. And you can see, the CTC, both the DoD and the NCTC are over to the far right in terms of being more costly than the other strategies on the efficient frontier.

You also can see that the life-years gained, as we just showed, are very similar to that in the higher echelon towards colonoscopy. This NCTC is not the same value. It's a little bit lower. So we can

see that we have life-years gained being good, but the cost is definitely high.

So what's happening here? Why is this happening? For CTC, it's a two-step procedure. You do a procedure, and then you're passing on people that are positive to colonoscopy. And you're repeating that every five years. Colonoscopy is a repeat every ten years. So that's sort of the basic difference in why this is happening 'cause you think it's a really good procedure, but why is it more expensive?

Also, just to point out to you, that the -- the X-axis starts at $1,900 dollars. That's not zero. So it's not zero/zero right there. So it's not that far off.

So the next thing we're going to do is we're going to talk about how to move the CTC value over to the efficient frontier. So the threshold unit costs for the base case. For CTC strategy our base case, six millimeter cut point and a five year repeat will be $199 dollars using the DoD study and $183 dollars using the NCTC study. Whereas the base case we were

starting with was $488 dollars.

We also, for the secondary analysis, looked

at what would be the value if CTC had equal value to colonoscopy. And that would be slightly higher, $221 dollars and $227 dollars. So not -- more in the $200 dollar range.

So let's look at some sensitivity analysis. And let's look at the threshold values by the screening interval and the lesion size triggering colonoscopy. So we have over here to the left is the base case. And then we see if we look at a six millimeter cut point with a ten year repeat, the cost per scan would be higher, $266 and $241.

If we use the ten millimeter cut point rather than the six, but did it more frequently, five years, it's about the same, a little bit less than what if it was six millimeters and five years.

And then the final one was ten millimeter cut point with ten years, and the value per test would be a little bit higher for DoD and lower for NCTC.

Let's look at the question of the adherence

assumption. So what we've done here, originally we started with 100 percent adherence. We're now taking

all other tests to be 50 percent adherence, and we're saying half the subjects are completely adherent and half won't come at all. So what would happen there?

So our base case stays the same -- this is just from the DoD study -- at $199 dollars. But if you looked at -- if CTC had a differential adherence of an additional ten percent, so we went from 50 percent to 55 percent, then the threshold costs would be $408 dollars. And if, indeed, the differential adherence was 25 percent greater so that we went up to 62.5 percent adherence, we would go up to even $694 dollars.

So why is this happening? Again, we're talking about a strategy. And the strategy includes getting people to go for care. So in this situation, you're relatively -- we know that the life-years saved is pretty close to that for CTC to colonoscopy.

And so if you have that differential in adherence, you move your life-years gained a little

bit higher, moving that point closer to that that we had for the colonoscopy point. So that's the reason

that the adherence is really such an important issue in terms of the cost-effectiveness analyses.

Then our final sensitivity analysis is this comparison among the three models. Are we consistent here? So in the base case I gave you before with SimCRC with $199 and $183, MISCAN is lower in terms of the price per scan, $122 and $108, and the CRC-SPIN is $196 to $205. There's some variation in there. But the results in terms of the life-years saved and also the costs are very comparable.

So what are our conclusions? The first thing is that CTC provides a benefit in terms of life-years gained compared with no screening. If CTC is performed every five years with that six millimeter referral threshold, life-years gained is slightly less than with the colonoscopy screening every ten years.

However, CTC is not an efficient screening strategy when that cost is $488 per scan. The threshold analysis indicates CTC every five years with

20 a six millimeter referral threshold could be efficient

21 if the cost is $108 to $205 per scan, depending on the

test characteristics and the model.

The higher cost per scan can be supported if adherence with CTC is better than that with other tests. So that's the hypothetical. And then finally, despite the differences across model results, our three independent microsimulation models reached similar conclusions.

Thank you.

DR. MC NEIL: Thank you. Do we have any questions for Dr. Zauber? Steve? Steve and then -- Steve, Cliff, Bob.

DR. PEARSON: That was a tour de force, and it was a quick tour. I think Barbara called you before and said we want our time to talk.

DR. ZAUBER: You did.

DR. PEARSON: So thank you very much.

First of all, I think it's fantastic that there are examples like this of doing multiple different models as a form of sensitivity analysis.

Just politically, though, I'm not sure you want to call them SPIN and MISCAN and things like that. You

probably want to call them more politically acceptable names.

The one thing, just to confirm, the CTC effectiveness looked, as you said, virtually -- or comparable to that of colonoscopy and higher than or comparable than the other noninvasive approaches, correct, on a life-years gained basis?

DR. ZAUBER: What happens is that the -- if you do a hundred percent adherence, if you do flex sig followed by -- with the annual FOBT, it really does quite well. That's assuming a hundred percent adherence. So those strategies are quite good also for life-years gained.

DR. PEARSON: Okay. But it's right up there, and it's higher than --

DR. ZAUBER: It's high.

DR. PEARSON: Okay. The other just question I had or comment, I suppose, is, I know you were asked to focus very specifically on the reimbursement cost

for CTC as a variable in the sensitivity analysis. It makes me a little bit uncomfortable because, as you

and I talked actually before the presentation, a lot of it is pegged to the relative ratio of reimbursement for CTC as opposed to optical colonoscopy.

And what your inputs didn't include were any anesthesia costs. Now, across the country -- in some parts of the country, the practice patterns are that virtually all patients under colonoscopy will have an anesthesiologist as part of the process. And they will be billed. They will bill as well. And so the cost for colonoscopy can vary dramatically depending on the practice patterns in the community. So when there's no anesthesiologist at all, I think the numbers are -- you know, will hold up quite well.

But one way to also think about this is in the relative cost of CTC to colonoscopy. And this was very complicated. But in a very simplistic way, we're saying that the effectiveness of CTC is about the same as colonoscopy. And you have to do it twice as often, every five years instead of every ten. So my guess

is that the modeling will show that if CTC is priced about half as much as what you're paying for

colonoscopy in your market, that it's on the efficiency frontier. Would you agree with that assumption?

DR. ZAUBER: The numbers you just -- yeah. I mean, it's half as -- a little bit even more than that.

DR. GOODMAN: Can I follow up on that?

DR. ZAUBER: Well, it's $200 -- about $250 versus the -- it's not as high as half. It's a little less.

DR. PEARSON: In the ballpark again, if we're assuming that the effectiveness is the same and you have to do it twice as often. Again, just looking at relative costs, if optical colonoscopy is reimbursed at a thousand dollars in your community, if CTC costs around $500, I'm thinking it's going to be on the efficiency frontier.

DR. ZAUBER: And just do the calculations in terms of what we were doing, 48 versus somewhere

between the $500 and the $650.

DR. MC NEIL: Could you say that again? I'm

sorry. I didn't follow that last sentence.

DR. PEARSON: It's not exactly half.

DR. MOCK: But we're talking about effectiveness and efficiency and cost. And the effectiveness that was just referred to in the question is at the six millimeter or less threshold.

DR. ZAUBER: Six millimeter or greater.

DR. MOCK: Six millimeters or greater, not the ten millimeters or greater.

DR. ZAUBER: Correct. Our base case was for six millimeter referral with five year repeat. And that's the recommendation from the American Cancer Society, the American College of Radiology, and Multi-Society, and that's what we did.

But there is also data -- the threshold costs, if you did do a ten year repeat or a ten millimeter cut.

DR. MOCK: Thank you.

DR. MC NEIL: Cliff, did you have a

question?

DR. GOODMAN: Yes. Yes. Really two quick

questions. One has to do more with how CMS might use the results of your study. Your study along with the input from USPSTF and others and our discussion today is going to perhaps inform the Coverage and Analysis Group how to -- sort of what decision they ought to make.

Your cohort of interest is in a previously unscreened --

DR. ZAUBER: Right.

DR. GOODMAN: -- 65 year old U.S. population. And I'm wondering, would you agree -- or what do you think about the following, that by the time any such policy like this is put into place, certainly some group of Medicare beneficiaries age 65 and older will have had colonoscopies, some of them starting at age 50.

So is it appropriate to suggest that the utility of this analysis, assuming that it's well done, at least as quickly -- as I could follow your

quick description, it sounded good to me -- that the

utility of this analysis would be only partial for

making a decision that might apply to the overall Medicare population who by the time this policy -- some policy might be implemented will have had -- some sizeable percent will have had at least one colonoscopy.

Won't that be a -- your studies are only describing part of the beneficiary population about which Medicare cares. Correct?

DR. ZAUBER: We're starting at age 65. Yes. The exact answer to your question is that we are in the process of exactly evaluating that question. If you start screening at age 50 to 64, what's the impact going to be on Medicare?

DR. GOODMAN: Great.

DR. ZAUBER: We're in the process of setting that up, doing it, at this moment. So I do not have the answer for you, but it's definitely in the works.

DR. GOODMAN: I'm glad to hear that.

DR. ZAUBER: Okay.

DR. GOODMAN: That will better characterize the beneficiary population. So then the related

question -- since it sounds like you're going to use this model for other purposes or try to adapt it differently. You looked at CTC every five years, colonoscopy every ten, sort of largely independently. Could the models be adapted to look at more of sort of a blended approach such as you started out with your first colonoscopy, and if that had certain findings, then you might go with CTCs thereafter and various combinations like that?

DR. ZAUBER: The models certainly do that. We were not requested to do that in this situation. We did evaluate a fair number. But the models have no difficulty saying start with colonoscopy, then go to CTC, do it ten years, do it five years. That's the beauty of the models. You can work these things through using the sensitivities and specificities that you have.

DR. MC NEIL: Bob? Did you have a question?

DR. MC DONOUGH: Yes.

DR. MC NEIL: Just to be clear, Bob, Jed,

Steve.

DR. MC DONOUGH: I actually had one comment and one question. My comment was actually kind of along the lines that --

DR. ZAUBER: I can't hear you so well.

DR. MC DONOUGH: The comment I had was kind of along the lines of what Steve brought up. And that is, you know, we're monitoring at Aetna the expansion in the use of anesthesiologists with colonoscopy screening. I know in this report there was an assumption that there was not going to be any anesthesiologist cost.

But in certain areas of the country, primarily on the east coast, most colonoscopies, at least in our experience, are done with anesthesiologists and with anesthesiologist costs. And I think you can do what Steve has done, a back of the envelope interpolation of what the effect would be in terms of cost-effectiveness.

But I would think that it might be

interesting in a final report maybe to include that in your sensitivity analysis. You know, how would the

addition of an anesthesiologist cost to colonoscopy affect relative cost-effectiveness ratios so you could have something more --

DR. ZAUBER: That's certainly -- this is the draft report that's up on the website, and we certainly can add that additional factor in there. The data on costs that we're using is based on what we used for the stool DNA report which we did for ARC last year. And so it's on 2007. And we worked with CMS to get those costs.

And I specifically asked about the anesthesia, and I was told that it was not covered. And that's the reason it's not in our costs. But we can add that back in in terms of looking to see what that threshold would be.

DR. MC DONOUGH: Yes. There are some Medicare carriers primarily in the west that do not cover it. But I believe on the east, they actually have a different Medicare policy. So it varies from

different regions is my understanding.

DR. ZAUBER: Also what's not covered is the

prep. I couldn't find anything that covered the prep. So that seems to be a patient cost.

DR. MC NEIL: So why don't we go through a few quick questions now, if I could? Quick questions and quick responses. Jed, did you have one?

DR. WEISSBERG: Yes. Thank you, Ann. Excellent review. You look at just the variable costs of each of these tests and don't consider what it would actually take for an organized delivery system with the goal of increasing its screening for colorectal cancer to decrease mortality, what it would take to implement these various strategies.

There's very different resource implications and capital costs in building sigmoidoscopy rooms versus colonoscopy suites. Different manpower implications as well. Is that accurate?

DR. ZAUBER: Yes. We were asked to do this from the CMS perspective, what was the CMS costing, what would they be paying out. We also have a

20 societal perspective, a modified societal perspective

21 in the report where we include the copay and some time

for the test. But it does not include the -- you know, getting the story out. And it's $4.54 for a Hemoccult SENSA. So that doesn't include explaining how to do the tests. I agree.

DR. WEISSBERG: Right. And I guess from the CMS perspective, I think you said that the Hemoccult II test actually is cost saving in terms of lives saved?

DR. ZAUBER: Yes. But it's low -- it's the lowest of the low. So it's -- in fact, for the Task Force recommendation, we came to the conclusion that Hemoccult II by itself and flex sig by itself really was lower than the other screening options and that would not be so recommended.

DR. WEISSBERG: Right. So from the point of view that Cliff was mentioning, you know, we know from (unintelligible) data that, you know, upward of 60 percent of at least health plan covered beneficiaries are getting some form of colorectal cancer screening.

And it's interesting to try to find out from NCQA how that numerator is being satisfied, what

technique is going into that satisfaction. And as best as I can tell from a study that was in the American Journal of Managed Care, it was on the order of 35 to 50 percent were by a colonoscopy, and all the rest were by other techniques.

And to put that in perspective in our system of care, we were dissatisfied with our rate of about 40 percent screening, wanted to get it up to other kinds of cancer screening tests. Had flexible sigmoidoscopy, had some limited capacity for colonoscopy, built up our colonoscopy capacity, but really saw the increase when we started mailing out the fecal immunochemical tests. Had a dramatic response in return of on the order of 38 percent, which has dramatically elevated our screening rate, which is what we wished to see.

DR. ZAUBER: But you must have it more annually there. I mean, with the FOBT, it's a very good test, but it needs to be repeated and repeated.

DR. MC NEIL: Let's see. Steve Teutsch, I think.

DR. TEUTSCH: The other thing that was not included as I understood in the model was the costs of the additional evaluations for the extra-colonic findings. And assuming that the benefits and harms are a wash, did you have any estimate of what the costs would be and how that would affect the costing of CTC versus colonoscopy?

DR. ZAUBER: We did not include the extra-colonics. There are some cost data out, but they are just recently. Pickhardt has data on what would be the additional cost and a couple other estimates from that.

But we really didn't have a good estimate of the harm. So we could add it onto the cost, but we don't do anything about either increasing the life-years that person has or decreasing it.

We have perforation costs and bleeding costs on colonoscopy in the model, and that's because we both assigned a cost to it, and also, you know, if

someone perforates and dies, they're taken out, and that's a negative against colonoscopy. So the reason

for not having it in the model is that we didn't have how we could connect and change the life-year factor.

But again, it's something that could be added on to the CTC costs. But we didn't feel it was fair adding it when we couldn't give it a benefit.

DR. TEUTSCH: Right. But assuming that it's neutral, then the costs for CTC would look even worse than they do in your base case. That's correct.

DR. ZAUBER: I could call on Iris who's done our number crunching if you want to talk about the issue of adding on extra costs.

MS. LANSDORP-VOGELAAR: If there would be no benefit?

DR. TEUTSCH: Right.

MS. LANSDORP-VOGELAAR: It would lower the threshold.

DR. SINGH: I have a couple of questions. So you only looked at adenomas of six millimeters or more. What about the ones less than that? Did you

consider that some of those adenomas that presumably

would not be seen by CTC, would be missed, could also

become cancerous in the meantime?

DR. ZAUBER: Yes. I mean, the way the model -- what's so beautiful about the model is that they're natural history models, and then you overlay onto the natural history the intervention. And so we talked about the specificity both for colonoscopy, being picking up hyperplastics.

And we talked about the specificity for CTC, that it's going to have some false positives. And some of those false positives are going to be where they ended up being small adenomas picked up rather than the larger. You know, it turned out to be it was a four millimeter adenoma and not a six millimeter adenoma.

So you're going to pick them up there. You're also going to have people who had a large adenoma and two adenomas of size four millimeters. So those are going to be picked up, some with colonoscopy and some of those are going to be detected with CTC.

And, yes. It is modeled in because you're modeling in what's going to happen with CTC, who's

getting them referred. You model in what's then found at colonoscopy. At each, you've got a huge population simulated, and some will have no adenomas, some will have one adenoma, some will have multiple adenomas. And you overlay that. And, yes. You will be picking up some of the small adenomas by having the CTC referral.

DR. MC NEIL: Okay. Let's see. Gerald, were you next? Yes.

DR. PEDEN: Do you have more?

DR. SINGH: Yes. I just have one more, actually, comment. Barbara, here we now do have numbers for the six to nine millimeter --

DR. MC NEIL: Yes. Actually, let's ask her where they came from.

DR. SINGH: Right.

DR. MC NEIL: That's a good solution.

DR. SINGH: We were struggling earlier on and also on the bus as we were coming, that there are

not very good numbers that we could get for six to

nine millimeter adenomas on the sensitivity and

specificity.

DR. ZAUBER: So on both Pickhardt's data and on Dr. Johnson's data, they have per adenoma sensitivities, and they have it for greater than six millimeters and greater than ten millimeters.

DR. SINGH: Correct.

DR. ZAUBER: And so we summed in between. We took, you know, what it was for ten and then what it was up to six, and then you have your six to nine. Did I lose you?

DR. MC NEIL: So you had the raw data?

DR. SINGH: Mathematically derived. Exactly what we were talking about in the morning. They're mathematically derived. What you said was not --

DR. MC NEIL: So we didn't think those data were in the published papers. And we didn't have a chance to look.

DR. ZAUBER: I've got them with me. I'll show you the --

DR. SINGH: No. They're not in the published paper. But what she says is she got the

greater than six and greater than ten and then mathematically computed what it would be from six to ten. Which, you know, can have some problems with it. Better to have the real data if you could.

DR. MC NEIL: Okay. Quick comment from Steve Pearson. Oh, I'm sorry.

DR. PEDEN: That's okay. I just want to make sure that I'm understanding the interpretation of the adherence graph. I don't know if you want to flip back a couple of slides. But the sensitivity analysis on the adherence, you had started out saying that you assumed a hundred percent adherence. So can you just walk me through this slide that starts out with a base case of 50 percent adherence?

DR. ZAUBER: Right. So we looked at if CTC had a 10 percent higher adherence rate than another test. So 10 percent over 50 percent is now 55 percent. So you've got 55 percent adherence coming through for CTC, but only 50 percent for another test.

So considering that the life-years gained at a hundred percent adherence are pretty comparable,

you're moving up the strategy of CTC to higher life-years gained because more people have accepted to have this test than another test.

DR. PEDEN: Okay. So the more people that accept to have this test, the more you are able to support a higher reimbursement?

DR. ZAUBER: Differentially over another test.

DR. PEDEN: Got you. Thank you.

DR. MC NEIL: Hold on. By the way, unless there's an urgent need, I'm going to ask people to just take a break one by one because it seems to me this discussion is going well, and I don't know that there's any reason to get up and take a break.

Does everybody agree? So if you feel like going out and doing whatever, do it. Otherwise, we'll keep going.

So let's see. I have Curtis, I have Steve, I have Mike in that order. And I have David.

DR. MOCK: I'm a family physician and geriatrician, and I like to think simply. Did I

understand that the utility for this procedure as a screening test could reach the frontier if the cost were reduced?

DR. ZAUBER: Yes.

DR. MOCK: Thank you.

DR. MC NEIL: Well, that was easy. Okay. Steve? It's good to throw in an easy one every now and then. Steve?

DR. PEARSON: I thought Steve Teutsch raised a good point about trying to --

DR. ZAUBER: Here's the threshold. This is the threshold analysis at a hundred percent adherence. If you could move that back --

DR. MC NEIL: We got that, I think. Why don't we move on?

DR. PEARSON: Steve Teutsch's question about the potential costs of incidental finding workups -- and perhaps other people may want to correct me. But just to put some boundaries on that, it may seem like

it could be a lot. But the best data -- the largest

data published say that it's $2.34 per patient as far

as the workup of incidental findings averaged over all patients.

DR. MC NEIL: And where do those data come from?

DR. PEARSON: That's from a Kim article in 2007. The highest in all of the published literature we were able to find was from a 2003 study that said $34 dollars per patient. So the biggest, $2.34, the highest in any published data we found was $34 dollars per patient for the cost of incidental finding workups.

DR. MCNEIL: Just to clarify then, the Kim article is from that smaller radiology study?

DR. TEUTSCH: That's hard to believe, that the 15 percent rate means that 15 percent need some sort of an evaluation after a CTC and that can be done for pennies?

It depends what you do. But if you've got a large percentage with what seems to be significant

lesions that require some sort of a procedure, that just doesn't -- and I don't have the data, but that

doesn't sound credible.

DR. PEARSON: The group that did the largest study -- and again, this is Pickhardt's group in Wisconsin -- they used specific guidelines approved by the American College of Radiology for how you work up these incidental findings. And those guidelines are relatively clear that you don't have to work up everything you find. They only had, I think it was 8 percent incidental findings. And they didn't have to work them all up.

So anyway, I mean, that's what they published. I don't -- I obviously didn't see the primary data. But that's what was in the article.

UNKNOWN MALE VOICE: And that was the $2.34?

DR. PEARSON: Yes. $2.34.

DR. MC NEIL: Okay. I have Mike and then David.

MR. LACEY: Yes. I have -- this is a follow-up question on the importance of the adherence

point that you made of CTC versus others. Did you look at the cost-effectiveness or the cost per life-

year gained of colonoscopy and CTC against no screening in terms of a ratio?

'Cause based on that graph, you know, it would look as if colonoscopy would be around 25,000 per life-year gained, and CTC would be about 28 to 31 percent, 31,000 per life-year gain, which is well below an acceptable threshold for covered services, broadly speaking. And I was just wondering if --

DR. ZAUBER: It's in the report? Looking at the colonoscopy comparison?

MR. LACEY: Well, I was just ballparking it from there.

DR. ZAUBER: Okay.

MR. LACEY: 2800 to get 85 life-years, roughly. And that seems to be consistent with the ICR (phonetic) report from Washington --

DR. ZAUBER: Yes.

MR. LACEY: -- as well that reported, I think, in that range.

DR. ZAUBER: The SimCRC model is what was used for the ICR report. So it's slightly different

assumptions, but for the most part, they're going to be very, very close.

MR. LACEY: Right. So I'm just -- it would seem as if, given the level of uncertainty and the potential for, you know, this choice of a technology that is clearly at least as good as the best thing out there, it would seem as if it's cost-effective relative to no screening, provided you can have enough evidence that you're bringing new patients in for the test.

I think that's a very important policy issue that seems to flow from this analysis. It's pretty fascinating.

DR. ZAUBER: Our primary analysis was against all the other screening tests, and the secondary analysis was against colonoscopy.

MR. LACEY: Right.

DR. MC NEIL: So David?

MR. LACEY: So I'm saying against no

screening.

DR. ZAUBER: Yes. You can see against no

screening it makes a difference.

MR. LACEY: Okay. That's all.

DR. MC NEIL: David?

DR. SAMSON: Okay. The analyses were done without taking into account quality of life.

DR. ZAUBER: Correct.

DR. SAMSON: And I assume that that was because the quality of life impact on the screening strategies would be assumed to be so transient as to be unimportant.

But the area where I think that that may not be true is would be in the extra-colonic findings in that you may have patients who, you know, are being followed for long periods of time. They may have great anxiety over the significance of some of those incidental findings.

Would you comment on that?

DR. ZAUBER: We did not include qualities in this analysis. We are currently with Ontario, Canada

in an analysis that is going to include qualities.

And it's difficult to find the right data. So it's

not included here. It isn't -- I mean, any of the screening exams do require a certain level of participation, which you want to take into account and, obviously, the anxiety.

But we did not include it. We didn't feel that we had sufficiently strong data to include it at this moment.

DR. MC NEIL: Thank you.

DR. SAMSON: Thanks.

DR. MC NEIL: I'd like to say, just to wrap this section up, if I could. It strikes me this was an excellent presentation, and we had a number of questions about some of the details which, if we had read your report more thoroughly, we would have caught.

But it strikes me that there were several things -- at least two things that I heard, and I'd like to make sure that there were not more that the group was asking about augmenting your analysis,

forgetting what your guidelines were in terms of CMS recommendations.

And one was that you include the cost of anesthesia specifically in your analysis. And the second one was that you try to work up the costs of extra-colonic findings beyond perforation and bleeding. And the third one was --

DR. ZAUBER: Extra-colonics for -- we do have extra-colonics for, yeah, CTC.

DR. MC NEIL: Right. That's what I'm talking about. That's all I'm talking about and the anesthesia for colonoscopy. I don't think people are interested so much in the Hemoccult parts of things.

And the third one, I thought, which is what you said you're already doing, was starting the age 50.

DR. ZAUBER: There is an age 50 in the report.

DR. MC NEIL: Right. Okay. So here's the question on that because I confess to not reading it incredibly carefully. So you can come up with a cost-

effectiveness calculation that starts the screening at age 50 as a societal cost. And when you do that

screening starting at age 50, you're going to find some colon cancers that are then going to get pulled out of the system.

Medicare is then going to come along at age 65, and that's when the Medicare costs start. So when you track those 100,000 new Medicare patients who have actually been screened since age 50, do you reduce the prevalence or the incidence --

DR. ZAUBER: Yeah. Yeah.

DR. MC NEIL: -- so that you've taken them out?

DR. ZAUBER: The natural history model is a lifetime model.

DR. MC NEIL: So you start at age 65 with a new cohort?

DR. ZAUBER: Right. And also because of the natural history, you do the exam, you take something out, but you can have a new adenoma. And the models are clocking in those --

DR. MC NEIL: Okay. Got it. Was there

anything else that we would have recommended that she

consider in the model?

DR. GOODMAN: I had recommended that in addition to considering people that are 65 and older who have had colonoscopies or any sort of screening before as opposed to an unscreened population that the model might also consider blends of the two procedures about which we've been talking.

DR. MC NEIL: Oh, right.

DR. GOODMAN: Because as opposed to one versus another, there might be scenarios that could involve both of them.

DR. MC NEIL: There's nothing obligatory here.

DR. ZAUBER: Well, I can just say that if we add costs, we can do that relatively quickly because we (unintelligible) any of the outputs. But when you talk about changing the strategy, it means all new runs for all three models. And we have a deadline of three weeks to get this in.

DR. MC NEIL: Just so you know, we're not trying to make work for you. And we don't want to --

DR. ZAUBER: They're good questions.

DR. MC NEIL: And we don't want to change your deliverable schedule or deliverables. But what you should just get from this group is some thoughts that might come up for another.

DR. PHURROUGH: And just to clarify, this panel doesn't provide you deliverables. We'll have some discussion at a later time.

DR. ZAUBER: Okay. We know we have deliverables.

DR. MC NEIL: So this is just off the cuff. So you can just listen 'cause these might be comments that a reviewer might ask, for example, if you were to publish this or when you publish it.

Are those the major comments we had regarding -- okay. Well, with that, I think we'd like to thank you very much for an excellent presentation. And now we're going to move on to our public speakers. And we have seven of them. And we unfortunately, are

20 running a little bit behind.

21 I think Maria has told all of our public

speakers that we have a very, very strict time limit of six minutes per speaker. The red light will go on and the microphones will go off and the lights will go down and you'll be pulled off the stage no matter where you are in your slide deck.

So let's see. It's Dr. Smith from the American Cancer Society who's first.

DR. SMITH: Good morning. Dr. McNeil, members of the panel, thank you on behalf of the American Cancer Society for the opportunity to contribute to this important discussion. I don't have any slides, so this will go very quickly.

I am Dr. Robert Smith. I'm director of cancer screening for the national office of the American Cancer Society. I'm also co-chair of the National Colorectal Cancer Round Table, a national coalition of more than 60 public, private, and voluntary organizations and individual experts dedicated to reducing the incidence and mortality from

colorectal cancer in the U.S. through data sharing,

strategic planning, advocacy, coordination, and

leadership.

Early this year, the American Cancer Society and the U.S. Multi-Society Task Force on Colorectal Cancer, which is the scientific advisory arm of the AGA, the ACG, and the ASGE, issued a joint new guideline for colorectal cancer screening in average risk adults.

Previously, both the ACS and the Multi-Society Task Force had endorsed screening with stool blood tests, flexible sigmoidoscopy, double contrast barium enema, and colonoscopy. In 2003, both the ACS and the Multi-Society Task Force separately reviewed the data on CTC and concluded that there was insufficient evidence to recommend for or against the use of CTC as a screening test for colorectal cancer.

Four years later and based on a rigorous evidence-based process, the participating organizations concluded that the data were now sufficient to include CTC among the recommended

colorectal cancer screening options for average risk adults age 50 years and older.

The guidelines update also noted that the available evidence indicated very clearly that adults still vary in their preferences for colorectal cancer screening tests. And insofar as screening rates still are lower than feasible and desirable targets, which means in more direct terms that each year there are too many avoidable deaths from colorectal cancer and years of life lost, that providing a range of screening choices is supported by the evidence and is sensible.

Ned Calonge said that I oftentimes say that the best test is the one you get. Actually, Sidney Winawer was the first one to say that. And it's gets repeated quite commonly. We now even say that the best test is the one you get that's done well.

Moreover, while cost-effectiveness analysis has compared lifetime performance of one test over another, the near term future colorectal screening likely will evolve to hybrid strategies employing

different technologies over the life course based on age, gender, risk, and previous findings.

The ACS has submitted more extensive comments to the record, and these are out on the table at the entrance. And here we would like to provide commentary on some of the questions the panel will address in their review of the evidence today.

The guidelines review methodology placed a priority on studies in average risk adults that included follow-up colonoscopy to validate all screening tests. Optical colonoscopy is commonly described as the gold standard since it can provide both visual confirmation of the results of the test under evaluation and tissue for histologic review.

However, it is important to recognize that optical colonoscopy does not achieve perfect sensitivity. In community practice, a number of factors have been identified that are associated with less than optimal performance.

The health benefits of identifying and removing polyps are well established and are

associated with reduced incidence and mortality from colorectal cancer. This is particularly true of the

larger lesions which have greater malignant potential than the smaller lesions. The benefit is achieved for any screening technology that is sensitive for both invasive disease and adenoma polyps.

At this time, the greatest sensitivity has been demonstrated with optical colonoscopy and CTC. With respect to the accuracy of CTC by polyp size, we found sufficient evidence that CTC achieved equivalent performance to optical colonoscopy in the detection of lesions equal to or greater than ten millimeters in size which is conventionally regarded as harboring significant potential risk to justify removal.

In fact, studies to-date show that while CTC does not identify some lesions identified by optical colonoscopy, it has also identified some lesions not identified by optical colonoscopy. The sensitivity of CTC is lower for polyps six to nine millimeters in size, but still within acceptable ranges. And there is a threshold that updated guidelines established for

referral for follow-up colonoscopy.

It is generally agreed that polyps less than

six millimeters in size do not constitute a near term risk, and patients undergoing CTC who are found to have one or more of these polyps in this size range should not be referred for immediate or short term follow-up. However, for patients undergoing optical colonoscopy, lesions five millimeters or larger are commonly removed as a precautionary measure.

And while there is disagreement between proponents of CTC and optical colonoscopy over the management of lesions in this size range, there is agreement by the guidelines panel at this time that patients with six to nine millimeter lesions identified on CTC should be referred to colonoscopy.

The National Colorectal Cancer Round Table, which does have a very strong quality assurance subcommittee, will be convening a workshop to address the management issues for sub one centimeter lesions to outline a research agenda and to develop practice guidelines.

The question of comparability of net health benefit from CTC compared with optical colonoscopy is

difficult to completely answer at this time. The data, including the recent publication of the ACRIN trial results in the New England Journal of Medicine, demonstrate that the tests are roughly equivalent in the detection of cancer and advanced adenomas of significant size.

The rate of procedure-related adverse events appears to be lower with CTC compared with colonoscopy. Concerns have been raised about long term effects of radiation exposure. But while current estimates of the potential cancer risk and other harms related to low dose radiation exposures during medical procedures derived from linear non-threshold models based on long term outcomes --

DR. MC NEIL: Dr. Smith, could you wrap it up? You're running out of time.

DR. SMITH: I'm sorry. Let me just finish with a point that we think is particularly important.

In the guidelines update we stated there's a

critical need for standards, including training and

experience and formal quality assurance programs,

including regular medical audits for both CT colonography and optical colonoscopy. And without these programs, there will be a persistent uncertainty about quality at the community setting for both examinations. And without these quality assurance programs, there will be a persistence prevalence of sub-optimal performance in these tests.

The quality of mammography was measurably enhanced by the Mammography Accreditation Program and by the Mammography Quality Standards Act. And we think similar quality assurance programs ought to be developed and supported by payers and professional organizations to measurably improve the quality of both examinations in the community setting.

We think that they should find a way to find common ground on this setting so that we otherwise can have the ongoing surveillance programs to measure and address the uncertainties that have been raised today.

Thank you.

DR. MC NEIL: Thank you very much. Dr. Dominitz? And I would like to remind you that we all

have your slides, and we've had them, so that you can move along rapidly.

DR. DOMINITZ: I don't know if my slides will be put up there or not.

DR. MC NEIL: Well, we have them in the book. So why don't you just start?

DR. DOMINITZ: That's fine. Good morning. My name is Jason Dominitz, and I'm an associate professor of medicine at the University of Washington School of Medicine. I'm speaking on behalf of the American Society for Gastrointestinal Endoscopy. And I would like to thank the meeting organizers and the panel for giving the ASGE this opportunity to comment on this important issue.

Although CTC is a promising addition to available screening tests, it's our overall belief that it's premature to endorse CTC for average risk Medicare beneficiaries at this time for several reasons, including concern about the sensitivity for

flat or small polyps, limited data on community-based

interpretation, and unanswered questions regarding

radiation hazards, management of extra-colonic findings, appropriate surveillance following a positive CTC, and cost-effectiveness.

The ACRIN study reported per patient sensitivity for large polyps of 90 percent, though the per polyp sensitivity was 84 percent. This is a subtle, but important, distinction.

It's difficult to determine the per polyp sensitivity for polyps in the six to nine millimeter range from the study report, as has been commented on earlier today. But the sensitivity was considerably lower for these smaller lesions, and my estimation is that it's 58 percent from the table that was presented.

In a study of nearly 14,000 patients of all ages undergoing screening colonoscopy, approximately 9 percent will have their largest lesion being a six to nine millimeter polyp. Among these small polyps, 6.6 percent had advanced histology. This is important

because surveillance studies after polyps are removed

have shown that patients with advanced polyps are more

likely to develop interval lesions and cancer compared to patients who did have advanced lesions at base line.

Under current guidelines, these patients with advanced histology are recommended to have repeat colonoscopy in three years. However, if the sensitivity for CTC in this size range is poor, then many patients with significant lesions will be missed and would not be recommended to have a repeat CTC for another five years.

Importantly, as the prevalence of polyps and the risk of advanced neoplasia increases with age, the proportion of Medicare beneficiaries with polyps in the six to nine millimeter range and the proportion with advanced histology is likely higher than I just quoted.

Unlike the fecal occult blood test which does identify a focal lesion, CTC will prompt endoscopists to look for specific lesions which may or

may not be present. This may result in lengthy procedures looking for CTC findings that do not exist,

the so-called false positives. In the ACRIN trial, the positive predictive value for neoplasia on a lesion greater than or equal to six millimeters in size when seen on CTC was only 40 percent.

It's unclear how patients with a negative colonoscopy after a positive CTC should be followed as endoscopists and patients alike are unlikely to be comfortable with standard surveillance intervals in this setting. The ASG is also concerned about withholding information about polyps less than six millimeters in size from patients. Ideally, patients and their physicians should be informed of all CTC findings and have the opportunity to discuss the management of these findings. Withholding this information is inconsistent with the themes of transparency and patient participation in health care.

In addition, there are still questions remaining about the sensitivity, specificity, reproducibility of CTC in community settings. In the

ACRIN trial, the radiologists had read either 50 cases

or attended a one-and-a-half day training session.

And only the top 15 of 20 radiologists who passed the certification exam were invited to participate in the study. Hence, this was a highly select group, and it's not clear if these results can be generalized.

In addition, there's still questions remaining about the radiation risks. It's unclear what the potential for harm is as a small proportion of patients undergoing CTC may develop a radiation-induced cancer.

And I think this has been discussed in some depth already this morning. But I'll just comment on one thing, that the technology assessment by Zauber and colleagues commented that a CTC every five years between ages 50 and 80 may lead to an excess cancer risk of about .47 percent. And while advances in CTC techniques may reduce the overall risk, this hazard is still not well understood.

Now, there's been a lot of discussion about extra-colonic findings as well. It's noted that about

16 percent of patients undergoing CTC are expected to require referral. This will lead to more patients

being referred for evaluation of extra-colonic lesions than the number referred for colonoscopy. And while only a minority of these are of clinical consequence, they will result in further radiation exposure, invasive testing, and potentially significant morbidity.

Now, the ASG also believes that we need more information about the appropriate surveillance intervals after a negative CTC, especially when performed in the community setting.

I'll move on. One potential benefit of CTC is that it may expand our menu of options for colorectal scanning. However, the impact of CTC on this issue has not been well studied to date.

In a randomized study by Scott and colleagues offering individuals a choice of CTC or colonoscopy did not result in more screenings than offering either test alone. Unless adherence to CTC is considerably higher than adherence to all of the

other tests available, CTC is not cost-effective as noted by the model by Zauber and colleagues.

So in summary, although CTC is a promising addition to colorectal cancer screening, the ASG believes it's premature to endorse this new test for the screening of average risk Medicare beneficiaries. We do believe that CTC is an improvement over a barium enema, and should be used for individuals with incomplete colonoscopy.

However, further studies are needed to assess the sensitivity for flat and small polyps, to clarify the risk of radiation, to determine the effectiveness of community-based CTC interpretation, and to define appropriate screening and surveillance intervals. In addition, more research is needed to determine if extra-colonic findings on CTC result in a net health benefit for patients.

Thank you.

DR. MC NEIL: Thank you very much. Dr. Rex?

DR. REX: I'm Doug Rex from Indiana University. I'm here representing the American

College of Gastroenterology. I would like to echo the comments of the ASGE and amplify just a few points.

First of all, with regard to the ACS-MSTF-ACR guideline, I want to emphasize that there's a very low threshold for acceptance in this guideline. I was one of the co-authors of the guideline. I was the chair of the Multi-Society Task Force for six years. And we use a relatively low threshold.

For example, we included fecal DNA testing, a test that has no better one-time sensitivity than fecal immunochemical testing, costs about 20 times as much, and has unknown program sensitivity. Double contrast barium enema is in the guideline. We have seven different tests that are in the guideline. And I think that needs to be kept in consideration.

And I would like to address, I think, a relevant issue which is whether this is the right population, the Medicare population, in which to begin the CT colonography experiment.

I want to flip down a few slides and touch on the issue of polyp management. I'm trying to go a

little bit faster, if I can, through the slides.

Obviously, I'm limited here.

But when we are taking care of patients with colonoscopy, we are managing not only individual polyps, but what we refer to as high risk adenoma findings. And it counts not only the histology of polyps, but also their multiplicity.

And I wanted to show this data which is from a polyp database collected at Indiana University where we're looking at the prevalence of patients having three or more adenomas or an advanced adenoma five millimeters or smaller in size with no polyp of six millimeters or larger in the colon. And in a 50-year-old and older population, this is five percent of the cohort. And it's going to be higher in the Medicare population because they have a higher prevalence of disease. So I want to point out that we're making a major paradigm shift in the way we manage polyps when we use CT colonography rather than colonoscopy.

Another recommendation that's made by the ACR is to do CTC surveillance in patients who have one

20 or two six to nine millimeter polyps. And this slide

21 shows you that in this screening cohort, there's

another three percent of polyps who have no polyp larger than that and who have either three or more adenomas or an advanced adenoma that's nine millimeters or larger in size. And again, that percentage will be higher in the Medicare cohort.

So we're talking about a very large change in the paradigm of polyp management. And it has to be considered carefully whether this is the best group to start that in. Jason, I think, briefly presented the potential of this in terms of increased numbers of cancers that might occur.

Now, we at the ACG considered that everything about this test depends on adherence. If the test results in increased adherence, then certainly we will have many more patients undergoing removal of large polyps, and we should get decreases in the rate of colorectal cancer.

If, however, there's not an increase in adherence, and the test primarily displaces patients

who would otherwise undergo colonoscopy, or they get

the test, and they fail to get their polyps removed,

then we could actually have a negative effect on colorectal cancer incidence. And unfortunately, we have very little evidence about adherence.

And Jason mentioned this study, a randomized trial from Australia in which patients who were offered colonoscopy or CT or their choice, there was no difference in the number who actually underwent a screening test. So we don't have published evidence that it will have an improvement on adherence. And this is a critical issue to understand with regard to cancer prevention.

I want to touch on the issue of how clinicians are going to decide who will get a CT colonography. Some would say perhaps everyone should get it. Others might say in the spirit of increasing adherence that only those who have refused colonoscopy.

And an intermediate approach would be those who have a low pre-test probability of disease. That

is, they are unlikely to have large polyps that require colonoscopy. And modeling has been looked at

to suggest that a stratified approach in the screen would have sensitivity comparable to universal colonoscopy if you used CTC in a low-prevalence population.

But no one has suggested that the Medicare population is a low-prevalence population that would be unique group. But rather that group would be the ideal group for colonoscopy as the first strategy.

So our position about this is that there are some important Medicare-specific issues, the high prevalence of disease. We have data now from the German national screening colonoscopy study that advanced adenomas convert to cancer faster in older patients.

The prevalence of adenomas increases with age in a linear fashion. But the incidence of colorectal cancer increases in a non-linear fashion. And the only explanation for that is a faster rate of conversion from advanced adenomas to cancer in the

elderly. So the stakes in identifying and removing these polyps effectively are quite important.

And extra-colonic findings which have been an important theme this morning, that issue is going to be amplified because the prevalence of incidental findings on CT is also going to increase with age.

Thank you.

DR. MC NEIL: Thank you very much. Let's see. Dr. Baumel?

DR. PATRICK: Good morning. Hi. I'm not Dr. Baumel. But he represents --

DR. MC NEIL: Could you go to the microphone, please?

DR. PATRICK: I'm sorry. I'm not Dr. Baumel. I'm Dr. Amy Patrick. But I do represent Colon Health Center of Delaware and Colon Health Center of America. And Dr. Baumel asked me to give this presentation today.

I'm a clinical gastroenterologist in practice in Wilmington, Delaware. And I'm part of a six physician GI group in the community there. I am

the medical director of the Colon Health Center of

Delaware, which is the branch of our practice that is

now offering integrated virtual colonoscopy to our patients as an option for their screening. And I thank the committee today for hearing the presentation.

I feel that our experience is unique because we are, unlike the ground-breaking clinical CTC programs at Bethesda Naval and University of Wisconsin and others, we are the first community-based GI group to incorporate CTC into our GI practice and to get it reimbursed. We are being reimbursed by Blue Cross of Delaware.

We're developing a growing experience about the clinical aspects of CTC or integrated virtual colonoscopy and the patient response to it as a screening test. We have been open for three or four months and have screened about 300 patients and are rapidly accumulating, you know, a better feel for what exactly is going on in the community setting with virtual.

If you take home only one message from me today and from our experience in Delaware, it is that

surveys of our first 300 patients screened revealed that over 40 percent of those patients when surveyed said that they would have opted for no screening at all if they had not been offered the virtual.

And it bears repeating, something that is a critical issue. These people were on the screening sidelines. They were opting for nothing. When virtual was offered, literally within days and weeks, they came in and got screened. And this is also corroborated by the fact that the average age of our patients so far is 56 years old, they have been sitting around, unwilling to do the optical colonoscopy. When virtual became available, they jumped at the chance.

So we can, and perhaps we should, debate, you know, at length three millimeter polyps, the potential or theoretical risks of radiation. But I, and we, feel that if we're really serious about impacting screening rates for colorectal cancer in

this country, we have to make a decision, you know, of whether to offer virtual. If we're serious, really

serious about impacting the screening rates, we can't continue to keep doing the same thing and hope that we get different results.

In front of us we have a noninvasive test that is arguably as sensitive as the more expensive and invasive legacy test. We have that available. We have data that 40 percent of people, you know, said they wouldn't have gotten any screening at all.

So we feel, I feel, that we need to see the big picture here. Colon cancer is deadly. We're not screening enough patients. The population wants virtual when it's offered as an option. The screening rates go up, and you're saving lives.

So the focus of my comments are the two questions, number six and seven. I feel that our experience in Delaware can speak to these two questions. The first was the issue of whether or not CTC will increase the screening rates, and question seven, how do we make sure that the patients who

choose virtual and need polyps removed get their

optical and have those polyps removed.

If I can go to question seven first.

DR. MC NEIL: You have two minutes, just so you know.

DR. PATRICK: It's not going the right way. Oh, there we go. Okay.

So there are two ways to ensure that the people that need polypectomies and optical get them. The first here is what I feel is most important and the second is also important, but the key is the first one. If we reimburse CTC only in a setting where there is a coordinated process to offer same-day, same-prep, that will give the best opportunity for patients with significant polyps that are found on the virtual to go on to the optical.

Stand-alone centers that do not have this coordinated process are forcing a significant number of patients into a second prep. And as a gastroenterologist -- and I'm sure many of you have had colonoscopies -- having to face the potential for

two days of a prep is going to be a significant barrier. So it does a disservice to the patient. So

same-day, same-prep option.

Another option, number two, is a wonderful and an effective way to do it. It's what we're doing in Delaware. We're bundling reimbursement. We are including payment for a hundred percent of the virtual and a modeled percentage of the optical.

I'm going to move on. I wanted to just mention, with respect to the cost-effectiveness study, the numbers that were used there grossly underestimate the cost of colonoscopy that I'm familiar with. We get about $500 dollars for a facility fee, $250 for professional fee. There's about $150 in anesthesia costs. And fill in $50 for pathology, it's $900 dollars. So I think if you use that number from the perspective of cost-effectiveness, the virtual, you know, blows away the optical.

And then some surveys that were interesting that I alluded to. We asked people --

DR. MC NEIL: I'm sorry. You need to wrap

it up.

DR. PATRICK: Okay. 40 percent that were

surveyed said they would not have gotten screened. The reasons for selecting integrated virtual were noninvasiveness, avoidance of sedation and anesthesia, ability to drive. You can see by the last bar graph, they didn't necessarily want to drive to work, but they wanted to drive. And how many would recommend integrated virtual colonoscopy to a friend or relative, 86 percent had an excellent experience and would recommend it.

This is the summary. It gives you the option to avoid a lot of things you want to avoid. Bottom line is that more people are screened, and the cost of the screening event can go down. So screening saves lives, and virtual accomplishes that.

DR. MC NEIL: Thank you very much. Dr. Klein?

DR. KLEIN: Thank you for inviting me. My name is Mark Klein. I'm a radiologist in Washington, D.C., also on the clinical faculty of George

Washington University.

And since you have the slides, I'm going to

try and go pretty quickly and just get to the very important points. First of all, I don't take any reimbursement or any compensation from anybody to speak here or any other meeting. I think this is a very important issue, and I certainly wouldn't want that to cloud your interpretation of what I'm about to say.

So the advantages we know for virtual colonoscopy, CT colonography. It's safe, it's rapid, it's accurate. Kind of like I'm speaking, safe, rapid, and hopefully accurate. And I'm not sedated. And we will talk about extra-colonic findings. I'm glad somebody's laughing over there. It means you're paying attention.

How good is CT colonography? I mean, I think this horse is out of the barn. I don't believe we're still talking about this. This is a great test. It's highly sensitive, highly specific.

And I would say one thing. We assume that

colonoscopy is the gold standard. I've had a

colonoscopy. It's a great test in the right hands.

But it is not the gold standard. The gold standard is colectomy. We don't do colectomies.

And I would also encourage the panel to talk to -- some of you I know are primary care doctors. But talk to a bunch of internists and primary care doctors and ask them how many patients they've had in the last five years who have had colonoscopies within the last few years and then developed colon cancer two years later.

It's not a perfect test, and we need to keep that in mind. There is no such thing as a perfect test. And CT colonography gets extremely close.

And without spending too much time, I just want to talk about this one study really quickly. This was the study in the New England Journal of Medicine by Drs. Kim and Pickhardt that was published last year. And there are two similar groups almost the exact same size. They were not the same patients, but they were two very similar sized groups. They

found almost exactly the same number of advanced adenomas. But if you go to the number of

polypectomies, it was obviously much lower in the CT colonography group because only the ones that were felt significant were sent for colonoscopy.

But look at the last line. This is something that has not been talked about. Look at the number of invasive cancers that were found on that study. Optical colonoscopy found four, and CT colonography found fourteen.

Now, they weren't the same patients, granted. But it doesn't take a great leap to look at this and say, well, they found the exact same number of advanced adenomas, but one found almost three times the number of cancers.

In my experience of thousands of CT colonography cases, CT colonography will find, in my opinion -- this is just my opinion, but I think the data supports this -- more cancers. So although we're looking for precancers, looking for polyps, it's also nice to find the cancers when they're small. And you

can definitely do that with CT colonography.

And I will tell you that in my experience

and that of many other people verified by this study, that you will likely find more. This is something we don't talk about. But it's certainly very important.

We're not going to go through all this because you already have this. So we're going to go real quickly.

Okay. Study interpretation. This is interesting. You've heard about two-D interpretation, three-D interpretation. You have to do both. I actually teach the course at the American College of Radiology teaching radiologists how to do this. The big advantage radiologists have is that they can read CT scans.

But I would say to you, if a gastroenterologist is interested in learning to read CT scans, there's no reason they can't read virtual colonoscopies. If you wanted to make a commitment, most physicians are pretty intelligent, can learn. And I don't think we need to have a turf battle about

this. I always feel that what's best for the patient

will work out just fine. If you're committed to doing

what's best for the patient, it doesn't really matter what specialty you're in.

Just to show you, that's what a colon cancer looks like. We're now going to fly through these things, but I do want to mention something about flat cancers, which is coming up right there. So can we find flat cancers? Absolutely. Those of us who do a lot of these, I will tell you unequivocally we can find flat cancers.

Can we find all of them? Probably not. Can colonoscopy? Probably not. But the question of can CT colonography find flat cancers, absolutely positively. There's another one there, by the way. These are in the first 20 cases I did, as a matter of fact.

The polyps we find are identical. That was a question on one of your points. Is there a difference between the polyps we find on one versus the other? No. They're the same.

Let's talk for a second about extra-colonic findings. If you look at the best papers, which I

believe is actually Perry Pickhardt's paper about four years ago, only about four percent of patients have significant extra-colonic findings. And in the hands of people who are trained -- and remember, we're talking about training radiologists and gastroenterologists to do this -- that you should understand what needs to go on to further evaluation and what doesn't.

And what we're really finding are extra cancers, lung cancers, renal cell carcinomas, lymphomas, and of course, aortic aneurysms. Yes, you can find aortic aneurysms, and it does preclude the need for abdominal ultrasound. So someone who's had a CT colonography does not have to have an abdominal ultrasound to exclude an aortic aneurysm. That question came up earlier.

Now, here's an example of a 50-year-old guy. And you can see on the right kidney there's this big kind of round thing on the back. I don't have a

pointer.

DR. MC NEIL: That's all right. We can see

it.

DR. KLEIN: At any rate, this is a gentleman 50-some-odd years old. Came in for a screening colonoscopy. His colon was perfect. He had a five centimeter renal cell carcinoma. We want to find these things. We talk about extra-colonic findings like it's a bad thing. It's not a bad thing. It's a good thing.

We don't want to send people to get their renal calculi worked up. But trained people won't do that. But we do want to find these things. So extra-colonic findings are not a negative. They're a positive. And if any one of you had CT colonography, you would be thrilled to know that your two-centimeter or five-centimeter renal cell carcinoma was picked up because you were asymptomatic and your life would be saved.

So we should stop denigrating these. We should just train people to understand what they have

to actually work up and what they don't. But it's not a negative. It's a positive.

Radiation. I'm not going to speak to you about that except to say we use very low doses. We've had ours calibrated. The total dose is about seven to nine millisieverts. In the Medicare population, this is irrelevant. And we shouldn't be talking about it at this particular meeting. If this was a pediatric meeting, absolutely right. But this is Medicare population. This is not a factor.

Training is very important. 50 cases --

DR. MC NEIL: Try to wrap it up.

DR. KLEIN: Okay. Last thing. I'll make a couple of quick points, and I'm going to get off the stage here. Again, I want to thank you for listening to me.

I think the case has been clearly made. First of all, I don't think anybody in this room would voluntarily have a fecal occult blood test for three years in a row rather than a CT colonography. We talk about fecal occult blood tests, and there's some data

that really just shows that doing something is better than nothing. But CT colonography is way better than

everything else on the market except for colonoscopy, which it is really in terms of lives saved, certainly is good.

And one last thing I would say that there's really -- at this point, if you really want to do what's best for patients, I think this discussion really hinges on the fact that the U.S. Preventive Services Task Force could not make a recommendation.

This is a very excellent group of very erudite, well-intentioned people. This would not be the first group or erudite, well-intentioned people to have gotten it wrong. For instance, Alan Greenspan said, gee, maybe derivatives weren't such a good idea. Or how about that Iraq war thing?

So you know, there's a lot, a lot of data. I've been following this for ten years. I've been doing it for six years. There is no doubt patients want this. There is no doubt you'll have much more implementation of screening across the population.

You will absolutely find more cancers.

To me, there's really nothing to talk about

here. If the government doesn't want to spend money on screening, that's one thing. But if you've made the commitment to spend money on screening, this is a test that we should absolutely positively offer to everybody, and in this case, to the Medicare population.

Thank you very much.

DR. MC NEIL: Okay. Thank you. All right. Dr. Cash?

DR. CASH: Thank you. My name is Commander Brooks Cash. I do need to say right off the bat, I am an active duty commander in the U.S. Navy, and the things that I'm going to talk about, the views I'm going to express are not necessarily reflective of the DoD or the Navy. I'm going to share our experience at Bethesda. I'm also speaking on behalf of the AGA. I want to thank the panel for allowing me to talk today.

What I'm going to do today is give you very briefly an overview of our integration of CTC at the

Bethesda and the National Naval Medical Center

experience. Now, you've already heard mentioned

several times NNMC which is a tertiary care military medical facility located at Bethesda has a lot of experience with this. We were the centerpiece for Perry Pickhardt's DoD study that you've already seen multiple times this morning that was published in the New England Journal of Medicine.

After that study was published, we received some grant money from Congress, and we set up what's called the Colon Health Initiative. We established this in 2005. Our mission was to increase colorectal cancer screening to our military medicine beneficiaries.

And the method that we chose to do this by was through an integrated CTC, GI, or colonoscopy program. This is administered by me in collaboration with my radiology colleagues. I'm the integrated chief of medicine at Bethesda and Walter Reed, and the chief of GI in the colon health initiative. And we share colleagues and resources through this entity.

Now, you've also seen a lot of this data.

I'm not going to belabor the ACRIN and the Pickhardt

study. I do want to share our experience with regards to the sensitivity of polyps greater than ten millimeters. It's about 94 percent. We compare that directly to our sensitivity for these polyps.

We are currently doing a 3,000 person prospective study. It's going to take eight years of average risk screening of CTC. And we are using segmental un-blinding very much like the original Pickhardt study.

For polyps six to less than ten millimeters, our sensitivity is about 84 percent. Colonoscopy with this realm or range of sizes is 94 percent in our study. I think we need to make sure that this is all considered relative to the data on sensitivity for colonoscopy, the current gold standard.

For polyps greater than ten, we know that sensitivity is somewhere between 94 and 98 percent. For all polyps, however, it's about 75 to 80 percent, similar to the data for CTC for polyps that are equal

to or greater than six millimeters in our current study.

Now, I've tried to address some of the questions that you're going to be considering later on this afternoon. Is there sufficient evidence to determine health benefits of screening with CTC using at least 16-slice scanners. And I don't think that we need to get so focused on the scanner slices because lower slice scanners are really not terribly available these days anymore.

Prior to CTC, no other approved screening test has shown diagnostic equality or equivalence to colonoscopy. CTC has shown this diagnostic equivalence in multiple large trials, as we've already seen that data.

I think a more apropos question would actually be compared to some of the other less invasive methods of colon cancer screening. How confident are you that there is sufficient evidence to determine the health benefits of screening CTC using at least 16 slice scanners for average risk

20 individuals?

21 And I really want to stress -- as a

gastroenterologist this is important to me -- that CTC should not be viewed as a replacement for colonoscopy. I've heard that several times this morning. I absolutely believe that this should be an adjunct to colonoscopy, and we should be reaching out to that other 50 percent of the population that is not getting the colon cancer screening that they should be getting.

What about polyp size, referral to colonoscopy, and intervals? I think polyp size and referral for colonoscopy are absolutely integral for the sensitivity of any noninvasive or non-polypectomy based colon cancer screening modality.

Current literature suggests that there is a very low prevalence of advanced polyps and a zero percent prevalence in patients with polyps -- of cancer in patients with polyps less than five millimeters. This is from a recent Lieberman and Eisen article in Gastroenterology.

We've already heard the data with regards to intermediate size polyps and, for that reason, our

recommendation and our practice at the CHI is to take all patients who have polyps greater than six millimeter to colonoscopy. And in our experience, we found that this is about ten to fifteen percent. Again, data that you've seen already today.

In terms of intervals, we don't know the growth rates. This is data that has to be determined. Right now, we believe that five year intervals are prudent until we get better data with regards to that. And we also, in addition to Wisconsin, are doing some natural history trials looking at leaving polyps in vivo for a year at our institution.

What about scanner resolution? I've already mentioned that our scanner radiation dose is about three to six millisieverts per CTC depending on the weight of the patient.

Adequate training has been touched on. As part of the -- a member of the CTC Task Force, we recommended 75 to 100 cases need to be done by

interpreting radiologists. We do believe the

radiologist or interpreter should complete a CTC

training course. The CT technicians, this is easy for them to pick up.

And also gastroenterologists can read this or non-radiologists. And we've done some studies with regards to that. And it highlights the relative ease of adaptation of interpreting these types of images.

Extra-colonic findings, just one brief comment on that. In our experience, it's less than five percent of our individuals who have gone through our study, more than 6500 CTCs in our experience, have had critical extra-colonic findings. And when we average the cost, it's about $20 dollars per examination added based on that.

More importantly, I think this is a central point that I do want to make here, is the compliance with colon cancer screening. I've shown here a graph of our HEDIS compliance. Without CTC added in, our compliance is about 63, 64 percent. When we add in CTC, our compliance goes up to about 74 percent.

We observed a 70 percent increase in colon cancer screening procedures at our institution with the

adoption of CTC.

And currently, we're doing about two-thirds the volume that we are for colonoscopy. And we've seen an increase in colonoscopies since 2005. We're doing more therapeutic colonoscopies, and we're finding more colon cancers at early, curable stages. But we've seen a steady rise in adherence with colon cancer recommendations.

I'm on my second to last slide. Current best evidence supports colonoscopy referral for polyps greater than six millimeters. That's what we do at Bethesda.

We feel very strongly a programmatic integrated program works. Same day colonoscopy, we want to minimize the prep. System tracking and call back of empaneled patients which will allow the opportunity for continuous quality assessment.

And in that realm, the AGA is recommending coverage with an evidence development process

requiring all performers to report into a registry.

And this will allow CMS to subsequently assess proper

training of physicians, proper equipment, natural history of diminutive and small polyps, the radiation risks, the management of extra-colonic lesions, and the system cost benefits when providing same-day CTC and colonoscopy.

And with that I will close. Thank you.

DR. MC NEIL: Thank you very much. Dr. Johnson? We'll hold our applause.

DR. JOHNSON: Good morning. Thank you very much for having me. I'm Dan Johnson. I'm a radiologist at the Mayo Clinic. I was a PI for the ACRIN National CT Colonography Study. And I'm speaking on behalf of the American College of Radiology.

The aim of the National CT Colonography trial was to evaluate the performance of CT colonography to identify patients that had at least one polyp a centimeter or larger using colonoscopy as the reference standard. We had 15 sites in the United

States that was comprised of both large and small

academic and private practices and recruited 2600

consecutive patients that were eligible for screening.

Reader training did occur, either by experience or a one-and-a-half day training course. And all participants were required to pass a test detecting 90 percent of adenomas a centimeter or larger.

We knew that we only had room for 15 of the 20 radiologists that were interested. It wasn't that they couldn't do the test or pass it eventually. We only had room for 15, so we took the top -- the 15 top scoring individuals into the trial.

The examination technical parameters are listed here. This was performed on a 16 slice scanner, and a low dose technique was utilized. All patients had colonoscopy, almost all of them during the same day.

Segmental un-blinding was not used for the reason that we were not trying to determine the performance of colonoscopy. We actually believe that

colonoscopy was the truth in this particular trial.

And we were looking at how well did CT colonography

compare to that. And I think that we were able to establish that as accurate.

You can see that 90 percent of the patients stayed. We were of average risk, and that there were 128 polyps that were a centimeter or larger in 109 patients for an overall prevalence of disease of 4 percent. There were 7 cancers in the study group.

Overall performance on those that we were most interested in were those adenomas that were a centimeter or larger with a sensitivity of 90 percent, a specificity of 86. The positive predicted value was 23 percent because of the low prevalence of disease, with an area under the ROC curve .89.

I'll be glad to explain the positive predictive value later with questions.

DR. MC NEIL: Just to remind you, we've heard a lot of these data. And you have only six minutes. So make sure you tell us what you want.

DR. JOHNSON: Their inter-reader variability

was low. In fact, 7 of the 15 readers had discovered

all of the polyps a centimeter or larger. Per adenoma

sensitivity is listed here that you've heard about.

So that the performance of colonography was similar to that reporting to colonoscopy for both large and intermediate adenomas.

If the target was set at six millimeters, we would send about 12 percent of the patients to colonoscopy. So that most patients would be spared the cost, risk, and inconvenience of colonoscopy.

There have been lots of issues raised this morning about the radiation dose. Remember that we used a very low dose technique in the five to eight millisievert range.

That has to be put in perspective to the other risks. Remember that the natural radiation exposure that we get is about three millisieverts at sea level. It's much higher at Denver. It's even higher in Santa Fe. And that airline personnel even get higher doses. And there's not an increased incidence of cancer in any of these groups that have

been studied.

In fact, the Health Physics Society and the

National Research Council have said that the small doses below those target numbers are either too small to be observed or non-existent or very small.

In fact, the evidence from seven studies evaluating nearly 100,000 workers of whom 60 percent have received doses above ten millisieverts have shown no statistical increase in cancer in those populations.

The linear non-threshold model we don't believe is an accurate representation of the low doses that patients intermittently receive because it's based on atomic bomb exposure of single, large doses of radiation.

It also doesn't take into account age, sensitivity to radiation -- you can see sensitivity really falls off after age 35 -- and target organ sensitivity which is much higher in the chest and head than it is in the abdomen and pelvis.

Finally, I want to say a little bit about

quality control. The ACR has put together a CT

colonography register under the National Radiology

Data Registry. They have identified a two process and four outcome metric.

Waiting times, that's a misprint. It should be we're looking at patient prep and CT protocols and well as complication rates, perforations that occur, true positive rates and false positive rates compared to those patients that go on to colonoscopy, and the percent of significant extra-colonic findings.

This has now been piloted at six national centers and will be available to the public for data registry beginning January 1. I feel that this is a very important part of maintaining high quality for the procedure. And I would emphasize that it may be important for you guys to consider adding the requisite of participating in this registry for reimbursement.

So in conclusion, CT colonography has performance that we believe is very similar to that of colonoscopy. Reader training is required. And there

are many national centers available for people to learn how to do this well.

Radiation exposure is small, and certainly the risk is much smaller than the risk of not screening for colon cancer or that associated with perforation. And that quality measures have been now adopted so that whoever does it, whether it's in a small community practice or a large academic institution, can compare and benchmark their results to national standards.

Thank you very much.

DR. MC NEIL: Thank you very much. So we're moving on to general public comments. I have -- let's see. I have six -- seven people here, and unfortunately, we have fifteen minutes. So you each have two minutes. I would strongly recommend that you not repeat any of the data that have been presented so far because you're really wasting your two minute time.

So, Dr. Donald Rucker from Siemens. If you'd like to come to the microphone. And if Dr.

Honinberg would like to get in line because we're going to move very rapidly right through here. And

then Dr. Fletcher, Brill, McFarland from the ACR, White, and Lau (phonetic). If you could just line yourselves up.

DR. RUCKER: Don Rucker, chief medical officer for Siemens in the U.S. I think I would encourage folks, the number of one in a thousand cancers has been raised a couple times.

And I think the BEIR VII study actually has fairly different numbers. It's quite non-specific when you look at it. But I think the lowest or let's say the worst radiation in adults is more on one in two thousand and again, there's, I think, very little evidence that any of this is happening without very long lead time. So not an issue for Medicare.

The other thing I would request for folks is I believe the colon cancer death rate is around 30 to 50 per 1,000. So even if you were to assume a 1 in 2,000 cancer rate down the road, I would certainly ask for that to be balanced.

Thank you.

DR. MC NEIL: Great. I'm sorry if I didn't

pronounce your name correctly. I couldn't read your writing.

DR. HONINBERG: That's okay. Good morning. I'm Robert Honinberg, chief medical officer of GE Healthcare. We would like to urge CMS to include CT colonography as an option for colorectal cancer screening for its Medicare beneficiaries.

Per the Balanced Budget Act of 1997, we appreciate that CMS is using its discretion in initiating its national coverage analysis and the MEDCAC panel to assess a technology that is at a mature state of technological advancement and is in the unique position of being validated by a large NIH-sponsored randomized control trial.

Per recently published joint guidelines, CTC has been offered as an option for colorectal cancer screening. We think it's fitting that this was a joint recommendation, given that the successful implementation and quality control of CTC screening

option will require the cooperation of multiple societies and stakeholders.

We support and are committed to an approach that requires specialized training of physicians and non-physician personnel for CT colonography. The successful diagnostic strategy is only effective in the hands of trained clinicians and staff, whether it is CT colonography or optical colonoscopy.

We also saw the work of the ACR and the AGA in developing accreditation for CTC, and we will continue to work with the professional societies to deliver effective training programs.

Thank you.

DR. MC NEIL: Thank you. Dr. Fletcher?

DR. FLETCHER: Thank you. I'm from the Mayo Clinic, and I represent the ACR. A critical question I think that we've heard earlier today is is CTC going to increase colorectal cancer screening compliance. And if it does so, it's going to increase the cost-effectiveness of the test across models.

And I'd like to point to the study of Darren

20 Schwartz, et al. from the University of Wisconsin that

21 examined the impact of CTC on endoscopic screening

volumes. You have this in your handout. And they looked at this in 2004 and 2005.

And they found that while endoscopic screening volumes remained relatively stable, there was a dramatic increase in total screening of about 70 percent, largely as a result of the large CTC screening program. And he concluded, quote -- he's a gastroenterologist -- "CTC has thus not replaced colonoscopy, but appears to have provided an additional screening option."

And from a clinician's perspective, for those of you that are clinicians, I'd like you to think about those -- that this is an important screening option, particularly to patients with barriers to endoscopic screening, the anticoagulated patient, the debilitated patient, the patient with sedation risk, the patient that has had an incomplete colonoscopy in the past.

So the second point I'd like to jump to is

the extra-colonic findings point that has been raised.

In your handout I provided a list of six large

screening studies and their rate of extra-colonic findings of potential medical significance.

Across studies, as you heard, this is about five to eight percent. And actually, the rate of extra-colonic malignancies of about .9 percent parallels that of localized colorectal cancer. About one to two percent of these people actually undergo surgery or therapy for the findings with a moderate workup expense of about $25 to $34 dollars as you've seen.

And radiologists have really taken a devoted -- are trying to minimize the potential morbidity and cost and maximize the potential benefit. Nearly all practices employ the C-RADS criteria for extra-colonic findings which really tries to emphasize the specificity of the finding so that only those where action can benefit the patient will be acted upon and minimize those that are likely unimportant. You have that in your handout.

Secondly, the ACR as you heard Dan Johnson point out, is establishing a database which will track

the percentage of extra-colonic findings of potential medical significance by participating practices whereby keeping it within established benchmarks.

Thank you for your attention.

DR. MC NEIL: Thank you very much. I think we're going to see if we can have the staff print out the slide that talks about extra-colonic findings. The color doesn't work on this particular -- I don't know whether we can or not.

MS. ELLIS: If he has the actual file. He brought those copies with him.

DR. MC NEIL: Oh, you brought this copies with you. We can't read your slides.

UNKNOWN MALE VOICE: (Unintelligible.)

DR. MC NEIL: Okay. That would -- okay. So it's Dr. Brill. Right?

DR. BRILL: Yes. Thank you. I'm Joel Brill. I am clinical assistant professor of medicine at the University of Arizona. I'm also the chair of

the Practice of Management and Economics Committee for the American Gastroenterological Association.

I'm not going to review all the information that's been reviewed. But I'll just simply make a few points. One is, what do we know? We know that barely half the people eligible for colorectal cancer screening have undergone screening by any methodology available. Therefore, we have a public health issue, and we have something that needs to be addressed.

CT colonography, if performed properly, can advance the goal of increasing colorectal cancer screening rates and can thus reduce the incidence of mortality for this disease. And the AGA would support coverage for screening CTC if CMS requires this to be implemented through CMS's policy, requiring coverage with evidence development, specifically a coverage with appropriate determination process.

We make the same recommendation to commercial payers. As being a former health plan medical director myself, I make the same recommendation to my colleagues as well, that if CTC

is covered, it should be done through a clinical

piloted trial policy because, as we've heard this

morning from the USPSTF, we do not have the answers.

What are the questions that a registry and CED would help us to determine? What is the natural history of small and diminutive polyps. What is the natural history of extra-colonic lesions? What is the natural history of radiation risks?

CMS could consider using the demonstration authority provided in MIPA to develop a CDC certification program. Specifically section 135(b) gives the Secretary the authority to conduct a demonstration project to assess the appropriate use of imaging services. Screening CTC for colorectal cancer could be designated as one of the advanced imaging services that can be included in such a demonstration project.

More importantly, CMS should define an appropriate episode of care for screening to ensure that an appropriate cross-specialty care model would be in place. The issues have been raised that when

the patient has a CTC on one day and a colonoscopy on another day, there is an increased cost and a risk to

the patient when they undergo two preps. Legislation should ensure that the patient can have those services performed and there is -- this is not a designated health service.

DR. MC NEIL: Are you wrapping up now?

DR. BRILL: Yes. I am.

DR. MC NEIL: Great.

DR. BRILL: Okay. Again, as mentioned, the comments should not be interpreted as suggesting that CTC should replace colonoscopy. As referred, colonoscopy is a one-step procedure. All other procedures that have been described are two-step procedures.

But given the gap in patient compliance with current screening guidelines, this could be an acceptable test.

Thank you.

DR. MC NEIL: Thank you. Dr. McFarland?

DR. MC FARLAND: Thank you. I'm Dr.

McFarland, radiologist from St. Luke's Hospital. And

I chaired ACR committee for colon cancer. You'll see

in my slides as I'll recap briefly that those refer to some more of the validation aspects. To start off with that, and the second part of this abbreviated presentation might be some issues regarding the modeling assumptions.

Briefly, beyond the ACRIN trial that Dan Johnson did present, was looking back at the cards, New England Journal article in 2003, Dr. Pearson raised the question about scanner issues.

That was done on four-D CT. And from the point of view of positive predictive value, that positive predictive value increased from that trial of 60 percent to the most recent trial that they published with OC validation. The first year validation was third-party payers in radiology to 90 percent, the difference being from four-D scanners to sixteen-D scanners that there's increased specificity, that you can see those aspects of focal pockets with an air to say that it's stool and not polyps.

So there is an advancement in the technology of scanners which is now widely spread out and that

has very much improved positive predictive value and specificity.

Briefly, you also mentioned in your report about the Mayo trial of 2007. This was 450-some patients that were asymptomatic. And the illustrations there describe both two-D and three-D comparisons that were similar.

I think there does need to be a clarification a little bit about some of the six to nine millimeter data which I think goes back and forth between two-D data and three-D data, as a point of clarification on the assumptions.

But if you look at the image, there were four out of five cancers that after CTC consensus went back to repeat colonoscopy and those cancers were discovered. One of those was a flat lesion.

And some of the issues with flat lesions are what is the diagnostic performance of any test. CTC in all of the validation trials to date has had very

important evaluations of what they have missed in terms of their false negatives. And there are no data

that show that it is the flat lesion morphology that has lead to these false negatives across all validation trials in terms of the issue about flat polyps that was briefly mentioned.

I won't go into the Munich trial. I know you mainly evaluate the U.S. trials. But the Munich trial of 300 patients that was recently done on 64 row scanner also had very high sensitivities to the smaller polyps of 90-some percent five millimeters and greater. And also there was a Korean trial of 1,000 patients recently published that you can see in terms of your results.

And lastly, just with great respect and thanks to the tremendous efforts done by the U.S. Preventive Task Force, two points of concern -- three points of concern. One would be just to better understand the six to nine millimeter sensitivity ranges that were used. There was a little confusion in terms of what was two-D data versus three-D data.

20 In today's world, it is a combined synthesized two-D

21 and three-D approach in terms of looking at those

estimates.

Secondly, what is the natural history of these small polyps in that modeling? From what we could see in our one-week review of this extensive document since it's November 12th posting was that 33 percent of diminutive adenomas may turn into cancer within 10 to 20 years. And forgive me if that isn't correct, but that was -- the transparency of what that figure is would be helpful. And it is somewhat skewed to start with 65 and greater patients in the Medicare considerations compared to the 50 and greater.

And thirdly, I would just say that the perforation rates also might need to be clarified among cohorts that were asymptomatic cohorts, screening cohorts compared to when we talk about perforations that affect asymptomatic or symptomatic symptoms of the perforation.

And the virtual colonoscopy working group of 11,000 patients, there were zero perforations in that.

The other trials had more symptomatic patients.

DR. MC NEIL: Thank you very much.

DR. MC FARLAND: Thank you.

DR. MC NEIL: Dr. White? No Dr. White? Hmm. How about -- I can't read the writing. Is it Judy Lau, Low, from Kimble and Associates? Anybody else? Last chance.

Okay. So then what we'll do is we will take a luncheon break on your own, downstairs or wherever -- although the wherever is probably pretty close -- till 12:35. And then the plan will be to have the presenters all here and for the panel to ask you all questions. And then the panel itself will have a discussion among ourselves with directed questions as needed to the presenters. And then we will take a final vote.

Are there any modifications to that agenda that we'd like to propose? Okay. Then I'll thank you. See you in an hour.

(Whereupon, a luncheon recess was taken.)

DR. MC NEIL: I'd like to have all of the

20 presenters sit in the front row so that it will be

21 easier for them to get to the microphone. Are the

presenters here? Are the presenters here?

Would you mind coming to the front row so we could -- so here's the plan. We have a time for questions to the presenters, time for deliberation among the panelists, and then time for a vote. I know several individuals have flights at 5:15.

UNKNOWN FEMALE VOICE: (Unintelligible.)

DR. MC NEIL: So what's the earliest flight, Maria?

MS. ELLIS: I believe 3:30. One of the --

DR. MC NEIL: Well, 3:30 we won't be able to do anything about, I don't think.

MS. ELLIS: That's fine. They go separately.

DR. MC NEIL: They'll get a separate car. Who's leaving at 3:30? He already left?

MS. ELLIS: No.

DR. MC NEIL: Who's leaving at 5:00 o'clock?

UNKNOWN MALE VOICE: You mean planes?

DR. MC NEIL: Yes, planes. Two people. How about earlier than -- later than 3:00 and earlier than

5:00? How about that? Okay. So we have two that have to leave at 5:00, which means they have to leave here at 4:00?

UNKNOWN MALE VOICE: No. It would have to be before that. 3:30.

DR. MC NEIL: 3:30?

UNKNOWN MALE VOICE: 3:30 I would say.

DR. MC NEIL: Okay. So we'll make sure the voting questions are done by 3:30. Does that sound right to everybody? So that would mean that we'll be efficient.

So first of all, I want to thank all of the speakers this morning for your terrific presentations. I think they were very, very helpful in illuminating the discussion material that we had already received. And everybody up here had spent some time reading it ahead of time, so I think that helped.

So what I'd like to do now is ask the panel members if they have any questions for those

individuals who spoke, either formally or in the public session. I realize we asked a lot of questions

while we were going along. Steve?

DR. PHURROUGH: Well, I'll ask a couple then. Part of the challenge in any new program that we put in place are the boundaries that we place around that particular program.

And as we've reviewed the data, as you've discussed the data, the various trials had somewhat different requirements and restrictions on how the procedure was applied. Do you use stool tagging and fluid tagging, different kinds of preps, excluding certain providers who don't meet certain requirements?

So as we make decisions around this particular technology, what sort of confidence should we have that the data that we are reviewing can be applied to a more general population of providers? And if not, should this particular technology only be allowed to be used or only be reimbursed in hands where the same kinds of restrictions that were placed in the trials would be placed upon those providers?

20 So --

21 DR. MC NEIL: Could I ask, when you're

responding, just give your name quickly so it'll be easier for our transcriptionist to know who you are. Just name is fine.

DR. PHURROUGH: So we had Dr. Cash, I think you were representing AGA. Could you give the AGA position on that perhaps?

DR. MC NEIL: Microphone please.

DR. CASH: Well, let me ask Joel -- I'm sorry. Brooks Cash. And I don't know if Joel wants to -- Joel Brill. There is he is in the back. So he may want to give the more formal AGA position.

But you know, our position and recommendation is as we suggested, that we at least be considered through a continuing evidence type of program. In terms of the confidence that you can have with regards to less expert hands, I think time will tell.

That was one of the rationale for the ACRIN trial. You know, I don't think that our data that we

present from Bethesda is necessarily representative of a center that's going to, first, be starting out, that

doesn't have two radiologists who have read over 5,000 CTCs. So there definitively is a learning curve.

I think that strengthens the need and re-emphasizes the need for appropriate training, appropriate qualifications. Whether or not it's going to be replicable or reproducible in the real world, I think remains to be seen. Although I think from the ACRIN trial that we get a hint that it probably will be with not terribly stringent or tough training requirements and competency requirements.

And certainly, you know, I think those should -- the bar should be set high initially. And then perhaps as we develop these things, that can be altered if it needs to be, or it can be -- you know, either up or down, just like we have with our endoscopic training models in the past.

DR. PHURROUGH: Are any of the ACR people still here?

DR. JOHNSON: Dan Johnson. I would really

concur. I think that the ACRIN trial has demonstrated

that of the 2600 patients there was only a very small

fraction of patients that weren't able to follow the directions for preparation. So I think it indicates that patients can do it and that it's easily transportable among a whole bunch of different practices, whether it's academics or private practice, large or small. So I think that that's fine.

I think the training issue, I think there are many good training centers out there. I think that it should be part of it. But I think, you know, it's really outcomes that we're looking for. And that's why I would really be trying to link this somehow to a quality database so that we can actually track, was the preparation adequate, was the CT technique followed, did we find those large polyps?

And then make sure that people are living up to the promise of this technique, which I think has been set forth by both the ACRIN trial, and the Pickhardt trial showed very similar data.

Does that answer your question?

DR. MC NEIL: Could I follow up on that while you're standing, Dr. Johnson? When you talk

about a database on quality, are you assuming that would be a self-funded, voluntary -- what exactly were you thinking about?

DR. JOHNSON: Well, I was referring to the ACR National Radiology Data Registry in which the CT colonography is a national database that they have put into place now. And it basically tracks those six, two process and four outcome, metrics.

How do you pay for that? Well, we need to -- that would have to be added into I think the reimbursement if we really expect people to follow this. I don't know what the charges for that would be. But it would be very much online with NQSA that are requirements for data reporting. And we all know how successful NQSA has been for breast cancer screening.

DR. MORRIS: I have a question for you on your criteria for submitting patients to the registry. Are there criteria for the centers to submit patients?

DR. JOHNSON: We're enrolling everybody that has the test.

DR. MORRIS: So conceivably, a radiologist could not complete the course and not do 500 preliminary readings with supervision, but still read these CTCs and submit to the registry. Is that correct?

DR. JOHNSON: I think that, you know, that would be one conceivable scenario, not an optimal one.

DR. MORRIS: No. Not optimal.

DR. JOHNSON: Yeah. I think optimally, someone would have training and then would go out and perform it on patients and would validate that their outcomes are acceptable with the CTC registry.

DR. MORRIS: So this would all be generated by the submitting radiologist or submitting center rather than a criteria, a quality control criteria by the registry?

DR. JOHNSON: Right. This is not by individual physicians, but by centers. So then the centers can kind of police those individuals and make

sure that they're actually achieving those high performance standards.

It may be that somebody isn't very good at picking up random uncommon events like polyps on a CTC exam. So those radiologists may be assigned for other tasks. And that way, they're going to be sure that the right radiologists are reading the rights tests.

DR. DOMINITZ: Jason Dominitz speaking on behalf of the American Society of Gastrointestinal Endoscopy. Coming back to your question about the data that's out there now and how might that apply to the general population.

You know, it is our concern that it will not be translatable into the general population necessarily. And that needs to be studied further. I believe -- and Dr. Johnson can correct me if I'm wrong -- that the rate of inadequate bowel preparations was very low in the ACRIN trial.

And in the registry data that he put up, it looked like a substantially higher proportion. And you can correct me if I'm wrong. I think it was

around six to eight percent had an inadequate bowel preparation. And there was percentage, I think

between ten and twenty percent where it was an inadequate examination overall. But please correct me if I misstate that.

UNKNOWN MALE VOICE: (Unintelligible.)

DR. PHURROUGH: You have to sit up here on the front row if you're going to talk. So come up.

DR. MC NEIL: Don't be bashful.

DR. PHURROUGH: We'll just make you stay up here now.

DR. BRILL: Joel Brill. I just wanted to go back to one of your earlier questions, and that's that both the radiologists as well as the AGA have issued standards and recommendations for training of physicians. Obviously, they have been society-specific.

The ACR recommendations, I believe, were a minimum of 50 per radiologist. The AGA recommendations which was a task force comprised of both radiologists and gastroenterologists recommended

an initial reading set of 75.

I believe that both of those emphasize that

there's an ongoing quality process as Dr. Johnson has mentioned. Certainly the AGA process has outlined that there's an ongoing mentorship program. So it's not that you're just trained and you're done. You're set loose. But there is an ongoing mentorship program to ensure that there's continual monitoring and measuring of what that physician is doing to make sure that they are adequate and appropriate in their ability to read.

The other thing was your comment about your 500. I believe the 500 cases do not refer to the physician. That actually may refer to an accreditation requirement.

As you may be aware, MIPA requires by 2012 that imaging facilities have to be accredited imaging facilities. And I believe one of the two accreditation entities would be the ACR, that's where that 500 number comes from.

There's also a second accreditation facility

called the Inter-Societal Accreditation. And I don't know what their exact number is. So we have to be

careful that we're not talking about physician. Physician and facility accreditation are two entirely different things.

DR. MORRIS: That seems a little confusing.

DR. MC DONOUGH: The facility has to have 500, not the physician?

DR. MC NEIL: Can you talk into the microphone?

DR. MC DONOUGH: The facility has to have 500. Is that what you're saying?

DR. BRILL: If I'm not mistaken. I know there's some ACR people here. But I believe under the ACR guidelines that the facility accreditation is 500. But if I'm mistaken, I will stand corrected.

DR. MC NEIL: Can we determine that, ACR?

UNKNOWN MALE VOICE: I'm not familiar with that accreditation standard. I know that for the ACRIN study that we said that readers had to have read themselves either 500 cases or participated in the

training session that was one-and-a-half days.

I don't think -- Beth was head of the colon

cancer committee or J.G., you want to speak up? I'm not aware of any accreditation for the ACR.

UNKNOWN MALE VOICE: So there's been a little confusion over the training by the societies. And I participated with the AGA in creating their standards. I trained the ACRIN readers with Dan.

And I participated in the recent update of the ACR standards. So I'd like to clarify what those are. So the AGA standard is that you read 75 cases with endoscopic correlation. And that thereafter, you have four to six weeks of metric training.

The ACR practice standard update is that if you do a lot of abdominal CT, then you read 50 cases with endoscopic correlation with cases carefully selected to reflect a wide range of morphologies of polyps and cancers. And then you have a quality program after you go back to track your patients that you refer onto endoscopy for exam quality and to follow up positive and negative lesions.

For the ACRIN study, what happened is that you're categorized as experienced if you had read over

500 cases. If you had read fewer than 500, you participated in a training course.

Now, the logistics of that training course were such that before people took the exam, they actually only reviewed 16 full data sets. Okay? So some people did not meet the threshold criteria after evaluating those 16 data sets.

So thereafter, we gave them training with 30 more cases, so they read 45 cases in particular. And all of the 15 ACRIN readers that participated in the trial read those up between -- the inexperienced readers read between 15 and 45 cases. They met the performance threshold.

And when we examined the performance of that pre-test of just 20 cases to their overall performance, there was no statistical significance in the difference between their prospective performance and the study.

Does that clarify? So there was some

confusion over people failing the test and people did not perform well after 15 cases. But that 15 cases

isn't the experience threshold that neither the AGA nor the ACR sets.

Does that answer any confusion?

DR. MORRIS: I have another question about the training. Did you -- for the radiologists and gastroenterologists that were being trained, they were blinded to the results of the colonoscopy before they read the CTC?

UNKNOWN MALE VOICE: For the test?

DR. MORRIS: Uh-huh.

UNKNOWN MALE VOICE: Yes.

DR. MORRIS: How did you ascertain that?

UNKNOWN MALE VOICE: Well, there were largely cases from my institution. And for the one radiologist from my institution, I made sure that he hadn't seen these cases.

DR. MORRIS: And the other, the other radiologist in the study?

UNKNOWN MALE VOICE: Well, there's one other

-- there were 14 radiologists from other institutions.

So they obviously hadn't seen the Mayo cases. So they

were all blinded to the cases. Correct.

DR. MC NEIL: Identify yourself.

UNKNOWN MALE VOICE: I'm Bob (unintelligible). I'm from George Washington University and also here with the ACR. I was the prior chair of CT accreditation for the ACR actually. And I just wanted to clear up some of the confusion about the site versus individual.

We don't currently have a CT colonography accreditation program per se. We have allegation overall CT program. And CT colonography will be created as a module of that program in the future. As part of the overall CT accreditation, we have requirements for sites as well as individuals, but individuals who read CT at an accredited facility. So the individual physicians have to have read 300 cases if they're board-certified radiologists. And if not, 500 cases as part of their experience.

So that's where that -- those numbers often

do get thrown out also. But that's referring to the

individual, not to the site. It's the individual

readers within that site.

DR. MC NEIL: And that's in place now?

UNKNOWN MALE VOICE: The full CT program is in place now. We don't have the module for CT colonography in place yet. And we're also just piling CT coronary angio which is --

DR. MC NEIL: Do you have any idea when we'll see a module for CT colonography?

UNKNOWN MALE VOICE: Again, it has to go back to the (unintelligible) council for approval. So that's probably going to be, I'd say 18 month type time frame.

DR. MC NEIL: Steve, did you have a --

DR. TEUTSCH: On a different topic.

DR. MC NEIL: Okay. Are we all finished with this topic?

DR. KLEIN: Mark Klein. I just wanted to comment on the training because we've -- this question has come up many times, and it's critically important.

And I think you want to be judicious.

I think training -- for instance, I teach.

I'm one of the instructors in the ACR accreditation course -- certification course for CT colonography. And it's not just being able to find polyps. We also teach them how to properly prep the patients, how to properly insufflate the colon. These things are critical. Finding polyps is probably the easiest part.

And when learned good technique, the success rate is very high. However, you brought up the question of whether or not we should require tagging, for instance. And whereas right now, I tag everybody. And I encourage the students in this course to tag everybody. Yet it may be that six months from now or a year from now as electronic techniques change and so on, this might change in a very short time.

So we wouldn't want to have -- I don't think you'd want to have it too restrictive. So you want to make sure people are trained in terms of how to do the whole procedure, not just identify polyps. But in

terms of being specific about whether you should need

tagging or not, I wouldn't like to see that in any

kind of document. That would be very hard to change 'cause technology, as we all know, evolves very rapidly.

DR. PHURROUGH: Just one final comment on this issue since this is a challenge for us routinely. It's pretty difficult for the Medicare program to come up with a policy that says this is new. We need to train those who are going to perform this procedure so that they're competent. And oh, by the way, Medicare, we want you to pay for it while they're incompetent.

It would be kind of difficult. And if we're not going to pay for the training, then that leaves it to Bob and Jerry and Curtis and all of their insurance programs to pay for the incompetent ones to become competent, then we'll start paying for it.

It's a challenge. We always have that challenge any time there's a new technology of who's going to pay for all -- you know, how many people are going to be wanting to be certified to do this across

the country? Say it's a quarter of a million. Fifty

cases times a quarter of million, that's a lot of CT

colonographies that are going to have to be done.

UNKNOWN MALE VOICE: Well, one good point about CT colonography is that the training can be virtual because unlike endoscopy where it's a hand-eye coordination, your interrogation of the colon is electronic. So the training can occur at any number of CME courses where people do sit down, investigate their own cases, you know, 700 slices using their own three-D data with endoscopic correlation.

And that interrogation to find the polyps is the same whether or not the patient is still on the CT scanner or whether the patient was done two years ago. So in this instance, the people that are seeking certification should be able to pay for their own training. And that really be done with a minimum of cost without Medicare having to shell out a dime to -- for patients at their own institution.

DR. MC FARLAND: Beth McFarland from ACR. Just to dovetail onto that, currently now there are

multiple societies that give multiple training courses

over the last two years. The Society of GI Radiology,

the FCDT, the ACR, as well as individual university programs.

And there are databases that exist of 50 plus cases -- Mark Klein was just referring to this -- endoscopically proven. And those same databases can be used again in terms of that setting. Any of these databases cover a very central core of specific morphologies from polyps to cancers to flat lesions.

If this is to be reimbursed, they will get themselves trained. Radiologists, gastroenterologists, others involved will get trained if there is that reimbursement on their own behalf. So I don't think that's something as a cost consideration.

DR. MC NEIL: Let me ask the panel here, have we done enough on training? Do we think we have it? Should we move on? Okay. Good. Steve, did you have a different topic?

DR. TEUTSCH: I wanted to turn to the

adherence issue a little bit because it's --

DR. MC NEIL: To the what issue?

DR. TEUTSCH: The adherence issue. And one of the places where adherence can become a problem, of course, is if people have findings on CT and then don't return for colonoscopy. And we heard that at least in some places, folks are set up to do them all on the same day. That's clearly not true around the country.

But since there's likely to be attrition, there's clearly a reluctance to have two bowel preps, there are the logistic issues for patients.

And without trying to get into the logistics of CMS and how they pay for this, how realistic is it for -- outside of sort of very specialized centers to actually have it set up so that you can get your CT and colonoscopy, if necessary, in the same day or within a reasonable period of time in the same day?

DR. CASH: I'll address this 'cause this at Bethesda is what we've done all along. For us, it's very feasible. Now, we are not a for-profit type of

organization. But we are a very busy endoscopy center. We're doing probably 6,000 endoscopies a

year. And what we do is, we shoehorn people in. Sometimes they'll have to wait an hour or two, sometimes four, before they get their colonoscopy.

I think with the adherence, the first part of your question, loss of follow-up if they have a positive CTC. What we found and we've asked patients who were reluctant to come in and get screened, but saw the CTC as a more attractive option because of the less -- the lower risk, the lack of sedation, that sort of thing.

They become very motivated to get colonoscopy when we tell them that we see a polyp on their CTC, and we show them the picture of the polyp on their CTC. So adherence, I think, in follow-up for a positive CTC is probably not as much of a worry as we would be -- we really would be worried about.

We do have some patients who do not come back. And those patients, we send them registered letters and prove and document in their medical record

that we've done everything we can to get them in short of dragging them in.

DR. TEUTSCH: This has been historically a big problem for mammography and things like that when you need follow-ups.

DR. CASH: Okay.

DR. TEUTSCH: So it's not unique to this. But because of the prep, it's even more of a problem. And so I was just wondering if CMS will only pay for it if you can do this, I don't know if you can even do that, Steve. But even if that were possible --

DR. PHURROUGH: Ask me on January 21st whether I can do that or not.

DR. CASH: The other thing that we will do for those people who we can't do a same-day, we'll keep them on a clear liquid diet. We'll bring them in the next day, and we will not re-prep them. And that has proven at our institution to be a viable alternative for those patients who can't do same day.

DR. MC NEIL: I wonder if we could follow-up -- and maybe this is just a derivative -- among

centers that don't have that immediate capability. We were talking about this at lunch. How easy would it

be for you to institute that capability?

DR. DOMINITZ: Again, I'm Jason Dominitz. I practice at a VA medical center, so not relevant to CMS. But we have three endoscopy rooms with one or two physicians working at any given time, to try to shoehorn in another colonoscopy on an unpredictable basis would be difficult. Maybe not impossible, but it would be difficult. It would require moving around the currently scheduled outpatients and it would be a challenge. It's something that the VA is considering whether or not to have CT colonography. But this is one of the hurdles that we would have to address.

The other thing that's important to note is that one of the advantages of a test like fecal occult blood test or CTC is that the patient doesn't need to be prepared to have sedation during their screening. But if you're going to do same-day colonoscopy, then that patient needs to have a driver available to them to take them home if they do get colonoscopy with

sedation.

So that does create another barrier. You

now have to have that driver ready with you when you go to CTC 'cause there's a one in eight chance or whatever that you're going to need that.

DR. MC NEIL: Okay. We have a whole bunch of people. Line up.

DR. BRILL: Okay. So I'm Joel Brill, and I'm in a community setting. I'm in Scottsdale. And Scottsdale is one of the centers that participated, as you may be aware, in the national CT study. There's capacity in the gastroenterology setting. I'll just leave it at that.

If you remember, 30 percent of colonoscopies done on Medicare beneficiaries are not done by gastroenterologists. 20 percent are done by general colorectal surgeons, 10 percent are being done by family practitioners and internists. That's Medicare data 2006.

So, you know, this is not -- you know, when you're looking at this, you have to not say this is

not just a GI/radiology issue. It is a all health care provider issue.

Yes. There are certainly parts of the country where this is a backlog, and there is a waiting time for people to get in for screening studies. And then there are places, probably 125th Street in Harlem where I'm sure I can get you in for a colonoscopy this evening.

So having the ability to be able to offer a same-day study, okay, is going to improve adherence and compliance. Anything that we do -- I mean, for any of you here who have had a colonoscopy, what was the worst thing about it? Let's face it. It was the prep. So if you're going to have to take the prep and have the ability to take the prep, take it one time, and get the study done on the same day, it's a benefit.

As for Jason's comment, yes. There are people who require sedation. Okay? There are also countries where the majority of colonoscopies aren't necessarily done with heavy duty sedation.

The comment was made beforehand by Dr. McDonough talking about Aetna data. If you look at my

article in Gastroenterology, Endoscopy Clinics in North America, where Aetna was one of the companies that was kind enough to provide us data that showed that there's a great variation in the use of deep sedation, monitored anesthesia care versus moderate sedation.

And it is a state by state, it is a community by community basis. If someone needs to be sedated and they don't have a ride, there are ways that we can do that. If it means keeping the patient until a ride can be obtained, okay, or arranging for other transportation, we've done that. We've done that for over 25 years time. And if we have to do that in order to encourage compliance, we'll probably do that in the future.

DR. MC NEIL: Other comments from groups that -- we're talking about the feasibility of setting this up. Not the desirability, the feasibility.

DR. REX: Doug Rex, Indiana. Surely there

will be lots of logistic issues because you have to

have a radiologist who's available to read the

studies, committed to doing them in a reasonable period of time. And then the endoscopy units, which are often very busy, are going to have to accommodate these additional people into the schedule. So it's going to require some gearing up.

And to extend the issue which is related to follow-up, I just want to point out, people are saying that the ACRIN trial and the Pickhardt trial are very similar. And in fact, they're not. And the biggest difference is in specificity.

The specificity in the ACRIN trial is considerably lower. This study is associated with a lot of false positives. And in clinical practice, when you have a patient referred with a polyp, and you perform a colonoscopy and it's negative, you're undone. You enter a world of uncertainty because you're dealing with a very specific lesion.

It's not like a fecal occult blood test that was positive, you did a colonoscopy, and it was

negative. There's a lesion on a study, and the

question is, is that lesion real or not. So now the

adherence issue becomes what are you going to do next? Are you going to trust the colonoscopy, or are you going to repeat another test? And which test are you going to repeat, the colonoscopy or the CT colonography? And is it going to be done on a different day?

So it's not necessarily done. We've dealt with this for years with false positive barium enemas because those patients had to come back many times. So I just say that when specificity is an issue like this, and we have lots of false positives, there's another element to this whole adherence issue.

And I think CMS may have to decide what's going to be done and are you going to pay for another study if it has to be done on the same day to verify whether a lesion is a true or false positive.

UNKNOWN MALE VOICE: I just want to comment on that and also what Dr. Rex just said. I do need to keep an eye on the ball. I think Dr. Cash and others

have demonstrated that the number of people that get

under the screening umbrella increases as you offer a

new modality, like CT colonography, that is highly sensitive for finding colon cancer.

So it's not a matter of either/or. We're now talking about people who are not getting screened. And if the goal is to find and prevent more colon cancers, then you want more people screened.

So in terms of adherence, I have patients -- and I'm going to answer your question specifically because I am in an outpatient facility, a private practice, with gastroenterologists within a few blocks of me. And I've talked to them, and they've agreed that any time we have a patient that wants to come over and have a colonoscopy following a positive CT colonography, they will fit that patient in. Now, that's not going to be universal around the country. You can also put patients on clear liquids overnight.

But I also have a large number of patients who say to me, you know, how big is this polyp? And I tell them, it's a centimeter or eight millimeters,

whatever. And they say, you know, I don't want to do this tomorrow. Do I have to do this tomorrow?

I say no, but it you don't do it today or tomorrow, you're going to have to take a prep again. Well, I'd rather just think about it, and I want to talk to this doctor or my cousin or my uncle who's a doctor. So not every patient is going to want to go on.

But again, I don't think these are really the sticking points. The point really is, if we want to bring more people under the screening tent to find colon cancer, don't deny something that we know for sure, for sure, works very well because there may be some issues.

There are issues in mammography you mentioned. I happen to do a lot of mammography. Every day I dictate a report and send out a certified letter for a patient who didn't come back for an abnormal finding on a mammogram. Now, remember, these are cancers in a mammogram. They're not precancers. If we find something on a mammogram, it's going to be

a cancer we're worried about.

We're talking about a polyp here. And we

all know that a polyp of one centimeter or smaller has one percent or less chance of being cancer. This is not an emergency like it is in mammography in a sense. So you know, again, let's just remember we're trying to get people screened.

And there will be issues. You bring up excellent points. But none of these are insurmountable, and all of them should take a back seat to ability to get more people into the screening tent.

Thank you.

DR. MC NEIL: Why don't we just have one or two more comments on this? I think we've got the drift here.

DR. PATRICK: Amy Patrick, community GI practice. I'd like to just say, if you came and saw, you know, how things worked, you would see that it's very streamlined and quite feasible from a gastroenterologist's point of view to have a same day

model.

Most GI screening is now in the hands of

gastroenterologists, and many or most of us are involved in endoscopy centers. We have one or two patients a day from the virtual center who need a colonoscopy, and it's quite feasible to add that patient onto the schedule.

It has not been difficult whatsoever because, you know, there are always cancellations and it's not a high volume of patients that needs the optical colonoscopy done. So GI docs are set up to accommodate that. And it really can be quite a streamlined, easy, good experience.

DR. MC NEIL: Do you have a quick comment?

DR. MC FARLAND: Just 20 seconds. Again, beyond the Navy's practice, also at University of Madison, Wisconsin, that do large volume -- I think they're up to over 5,000 now -- have very coordinated effort with gastro.

The point that Doug's just made about what do you do with that intermediate lesion that's

positive in one and negative in another test, whether

it be how you schedule patients that same day or how

you interpret these shades of gray of certainty, it takes collaboration. It takes collaboration between gastroenterologists, radiologists, and how do we communicate those results to surgeons and to primary care physicians?

So all this cohesiveness answers a lot of those different questions. And in programs that are doing high, high volumes, they're doing it well.

DR. MC NEIL: Thank you. Let's see. We'll start with Steve and then move down to Jon. Let's see, Steve, Jonathan.

DR. PEARSON: One of the questions we're going to be asked whether there's sufficient evidence for Medicare to make a judgement is this question of whether CTC improves population-based screening rates. And that was not part of the systematic review.

So to a certain extent, as a panel we're very reliant upon information that might be presented here today. And the only thing that I can remember

being published or mentioned were Dr. Patrick's comments, which I'm not sure were published, the

article that Dr. Fletcher mentioned, although I'm not so sure that that's a great estimate of its impact on a true population.

But I just thought I would invite anybody who knows of evidence that we should consider because we're going to be asked to judge whether there's sufficient evidence with which to judge this issue. Among those of you who consider it the main issue about CTC, we have to decide whether there's adequate evidence.

So can you help us with that?

DR. DOMINITZ: I mentioned the study by Scott from Australia which you should have in your slide which did not show any increase in uptake in an Australian population.

The data I mentioned earlier, about 40 percent of patients who had CTC said they would not have been screened otherwise, you have to keep in mind what population that was. Those were people who came

for CTC. It's not 40 percent of those people who have not been screened said they'd have a CTC rather than

something -- rather than no screening.

So I'm not aware of any studies that have really at this issue done well other than the Scott study.

DR. PEARSON: Can I just ask -- I'm sorry. You briefly mentioned the Scott study. Did they have a fixed population?

DR. SINGH: Describe the Scott study a little bit better for us 'cause I think it's a very important study.

DR. DOMINITZ: Doug, do you want to cover that in detail?

DR. REX: Sure. It's a randomized controlled trial done by mailing. Basically patients were mailed invitations to undergo one of three options, either CT colonography, colonoscopy, or they had their choice. The procedures were explained to them. And there were about 1200 patients. I shouldn't say patients. These were individuals. It

was random mailing.

And the end point was the number of patients

who actually underwent a test. And it was -- it ranged from 16 to 18 percent between the three groups with the group that actually was offered both was not the highest even in the 16 to 18 percent range.

I know there was discussion earlier of this paper by Schwartz that comes from the University of Wisconsin. And I just want to point out that when Perry Pickhardt went to the University of Wisconsin, the University was in an unusual situation of being two years behind on being able to do screening colonoscopies. So there was an enormous backlog of people that were ready to be screened.

Obviously, that's a situation where CT colonography is going to help get the job done in terms of screening. But I don't think that that's really representative of most practices across the country in the United States. When I talk to gastroenterologists, most people are no more than a few weeks behind on being able to do screening

colonoscopy.

DR. MC DONOUGH: Just to follow up. I

haven't heard this argument made. I mean, is there is a shortage of gastroenterologists?

DR. REX: Well, you know, others may want to comment on this, too. The CDC estimated that in 2002, we had about 14 million colonoscopies done in the United States. Their estimate, based on surveys, was that the capacity was about 22 million.

I think, like a lot of the phenomenon that we've talked about today, there are local variations, and there are places where screening colonoscopy is less available. I think it's become much more available in the last few years. And there are a lot of surgeons who are doing colonoscopy, especially in smaller communities. And in some communities, there are primary care physicians.

So I guess the ultimate question is, are there enough colonoscopists. And this probably depends on what source you look at. But according to the CDC, there are.

DR. MC NEIL: Let's see. Jonathan, I think you're next. Oh, are you --

DR. CASH: Can I just share -- yeah. If I could, just share our experience. I think the number of colons that need to screened is closer to about 40 million. So I don't think there really are enough colonoscopists to do a -- let's say we got a hundred percent adherence to colon cancer screening. We would not be able to do that with colonoscopists in the short term or even probably in the long term.

As I shared in my presentation in our personal experience at Bethesda, we've increased. And we do have a fixed population of DoD beneficiaries. We have increased our colon cancer adherence rates by ten percent according to our HEDIS compliance. And we do count CTC as HEDIS compliance. We have HEDIS with an asterisk for CTC for internal accounting.

So we've increased that to three-quarters of our enrolled population. Our (unintelligible) population is actually screened for colon cancer with the addition of CTC. And it nicely and totally

coincides with the initiation of our colon health initiative.

DR. SINGH: But there must also be other changes. I've worked a lot as an epidemiologist with (unintelligible) data. And especially (unintelligible) data from one center is not a controlled clinical trial. What Dr. Rex presented was randomized trial, patients are asked what they want to get. That's clinical evidence. That's epidemiology.

I go to a clinic, when I join a university, my interest is in gout, for example. I start seeing more gout patients. Patients know I like it. Does the incidence of gout increase in the population? No. It doesn't. I'm seeing more. But that's my interest.

Does a clinical do that? You may say yes. You increase the adherence, but there's not a control group. How do you know that the (unintelligible) was adjusting by itself because of the media quotes, or because everything going on, because of the presidential elections, because of (unintelligible). How do you know that?

DR. CASH: Well, I know that because I'm in charge of the gastroenterology division. And we've

actually lost gastroenterology personnel. So we have less people to do colonoscopies, and yet we're doing more CTC, we're doing more colonoscopies even with less people over the last three to four years.

DR. SINGH: But it still doesn't mean that -- what was the thing that increased the impact?

DR. CASH: It's advertising. It's a new test available.

DR. SINGH: Exactly. There you go. That's what it is.

DR. CASH: And a large portion of that is people coming in to get CTC. It's multi-modal, and that's all part of the same package.

DR. SINGH: But what I'm saying is, if you had a control group and you advertised that I bought a new colonoscope. This comes from Japan. It's gold-plated. It really helps. (Unintelligible.) (Unintelligible.) And I got very concerned that uncontrolled single-center experiences on

(unintelligible). And I have spent all of my life

doing this. I see this kind of stuff.

DR. PATRICK: Again, Amy Patrick. And I'm the one that only has the 300 patients. But we did do some surveying prior to opening the center to see if it seemed like the right thing to do. There's an overwhelming demand and desire for a noninvasive test.

DR. MC NEIL: I think the question is what has been the result of the desire.

DR. SINGH: Right.

DR. MC NEIL: Not what do people say, what do people do. Let's see. Jonathan and then Jed.

DR. WEINER: Barbara, I actually had the same question about population-based. And I won't ask it again. But I have a second one. It's clear that the evidence is modest at best or nonexistent. And as appropriate, I hope we can talk about how we can expand the evidence. But that's a longer issue.

The other has to do with -- I know that, you know, Medicare, of course, pays for a fee for service, CPT code at a time usually. But some of your

20 organizations, military for example, and we also have

21 some on the panel, Kaiser, operate a little bit

differently. I heard several speakers talk about an episode approach or thinking about it on a population basis. And not one or the other procedure, but a logical sequence of procedures, assuming, you know, we had the go-ahead.

I don't know of any advice from people that are already there that don't have to worry about the fee for service or any advice for us or Medicare how one might structure it within a fee for service system.

And also I would -- Jed, if you have anything from Kaiser that you would like to say about how one thinks about the episode approach.

DR. WEISSBERG: You want to come up here?

UNKNOWN MALE VOICE: No. You go first.

DR. WEISSBERG: Well, I indicted in my earlier remarks that we've seen a significant increase in our screening rate by a technique of mailing out fecal immunochemical tests, and we're getting a

dramatic response rates, positives, now adding to our

diagnostic colonoscopy queue which is squeezing down

on our screening colonoscopies.

So I think that when I talk to patients and offer them their choice of flexible sigmoidoscopy, fecal occult blood testing on a yearly or every other year basis, colonoscopy, I actually do mention that virtual colonoscopy is an up-and-coming technique not available in our system and actually not well established in our geographic area where I practice, and ask them what they want to do. And I'm constantly surprised that they choose one of the four. And that's their choice.

DR. CASH: Just in terms of how we structure the two together. You know, when people come to our center, they're coming to basically the gastroenterology clinic. We have a GI-driven, with our radiology colleagues, algorithm.

There clearly are people who are not right for virtual, and we steer them away from virtual. We don't steer anybody towards virtual or CTC. We

present the options for average risk individuals, and we let them choose. And we present what we see as the

possible advantages and disadvantages.

And we have some who choose traditional colonoscopy because they want one-stop shopping. They want to get it all done. And then we have others who like the option of possibly getting other organs looked at and extra-colonics, even though we stress that that is not part of the test, and we have a consent form that clearly states that. Or they just don't want to get the sedation. They don't want the inconvenience.

But we offer both in an average risk situation. And clearly, hedging towards safety and conservatism, pushing people, if anything, away from CTC who might not be appropriate for CTC.

DR. BARTON: Quickly.

DR. DOMINITZ: So two quick points. The mention about offering FOBT and other tests, at the VA we do very well getting the majority of our patients -- I believe it's over 75 to 80 percent of patients

are screened for colorectal cancer primarily through

FOBTs in a systematic approach with annual screening.

The VA has done quite well with this by using a systematic approach to screening without having CTC available.

Now, getting to your question about episodes of care, I'm fortunate in that I work in a salaried health care environment where we get paid not based on the quantity of work we do. And I am a little bit concerned about the idea of a proportionate payment for a colonoscopy.

We heard something about 20 percent of the colonoscopy payment, we would assume 20 percent would go to colonoscopy. Setting a threshold one way or the other would either lead to some pressure potentially of over-calling or under-calling lesions to try to meet that target.

So I would be worried about some kind of approach by Medicare. I'm speaking on behalf of myself and not the ASGE in this regard, you know, that it might lead to different call rates. I don't know

if that makes sense, but I hope you understand what

I'm saying.

DR. MC NEIL: Unfortunately, we do. I think.

DR. MC FARLAND: I just wanted to make one blunt comment. And that is, as we talk about where is the evidence in making evidence-based decisions, you are hearing from centers of excellence because there is not current coverage. We will never get to the ability to understand the generalizability into the community until we get coverage.

And so how do we get from that gap of centers of excellence which clearly are leading successful and collaborative efforts to the community, but providing a quality assurance program that helps and keeps safeguard over that in terms of quality of metrics?

DR. SINGH: No. My question or my point here is randomized blinded clinical trial where there's a center of excellence expert opinion. Armchair research, put your arms on a chair and make

an opinion, or go out and do a randomized trial.

And we are here to obviously evaluate the

randomized trial experience much more than an armchair expert opinion. And which we've done. Don't get me wrong. CDC has lots of good randomized clinical trial data. But it's just not (unintelligible) in every field. That's all we're trying to point out.

DR. MC FARLAND: And as you know, across fields and across technologies in today's imaging research costs, we don't have every randomized control trial to answer every question. And so you know, you're hearing about the need for colorectal cancer screening and what the capacity and the potential is here. So I appreciate your point.

DR. MC NEIL: Jed, did you have another comment?

DR. WEISSBERG: Yes. I just wanted to bring out one point on measuring the sensitivity. I think we heard that in the model that was employed in the exercise, it was a per-polyp sensitivity, and Dr. Dominitz was apparently supporting the idea of a

per-polyp sensitivity.

To me, it made much more sense to think

about it per-patient sensitivity, assuming that the colonoscopist does a full exam of the colon and doesn't just go to where the polyp might be.

DR. BRILL: Just one brief comment to Dr. Weiner's comment. In the commercial, non-Medicare world, there are many examples where the commercial environment allows us to adopt an episode of care methodology, bundled payments, and things of that nature, whether it's for endoscopic services, surgical services, case rates around diabetes care, congestive heart failure, transplant management, et al., et al. So the methodologies and the actual models do exist.

DR. BAUMEL: I'm Dr. Mark Baumel. I'm the CEO of Colon Health Centers of America. You heard from our first site.

Our whole entire business is built around putting these operations together. And I admit to you that it's not -- it's not a straightforward process to put together. But it's very doable.

And my fear is that if CTC is reimbursed just as a standalone test, you're going to have lots

of standalone radiology centers where there's an incentive on the other end, the incentive to not get the patient over to same day colonoscopy.

As you heard before, our entire system is built around an episode of care, a per screening event, a process. And we're paid for that per screening event. And that's, in my mind, the one and only way to guarantee that the appropriate patients who need optical therapeutic colonoscopy will get optical therapeutic colonoscopy.

DR. MC NEIL: Could we just go back to the per patient versus adenoma because I had the same question Jed did.

DR. ZAUBER: Ann Zauber to talk about the modeling. For our modeling, we model out the adenoma and the adenoma size. So for us, it was important to be able to look at this component and also to compare across both the DoD study and the NCTC, the ACRIN study 6664.

So the fact that we used a sensitivity

measure that was adenoma-based does not mean that we

didn't consider the patient. It's because the modeling has both the number of adenomas and the size of each adenoma, that's the reason we were doing it in this capacity. The patient-based is there. It's used. That's what you're getting out.

We've also done -- have just completed a cost-effectiveness analysis for 6664. I can't present those results. Another person is the first author. But I can tell you that our results were comparable for the NCTC study whether we used a more per patient sensitivity level or per adenoma. It's not -- it's not an issue in terms of you're getting similar findings either way.

Does that help?

DR. SINGH: One question I wanted to ask you. You used three different microsimulation models.

DR. ZAUBER: Yes.

DR. SINGH: What is the difference in the three simulation models?

DR. ZAUBER: The conclusions from the three models --

DR. SINGH: No. What was the technique? What was the technical difference? Did you put in different assumptions in the three models or what?

DR. ZAUBER: The models are developed independently in terms of the natural history. Then we're using common inputs. We're all standardizing, calibrating, to the adenoma prevalence data and to the (unintelligible) instance data in the prescreened population.

We have different assumptions about the dwell time. That's our biggest difference. And that's not something that we can really observe. And so there are some differences in the findings. And particularly from the MISCAN model, there's an assumption -- the dwell time is assumed to have greater heterogeneity, and it includes more faster growing cancers, more faster growing from the adenoma to the cancer.

And yet, the relative differences are

totally the same. All are showing that CTC is

definitely effective. All (unintelligible) have had a

colonoscopy. If you notice from MISCAN, we had a slightly lower price per scan because we weren't doing -- we were having more adenomas being developed sooner.

But it's very much standardized. It's comparative modeling. It's one of our best examples of a sensitivity analysis from the modeling point of view.

DR. SINGH: Thank you.

DR. BARTON: Other questions?

DR. DOMINITZ: Since you mentioned me, I figured I should say something.

The per-patient analysis is basically saying the screening is either positive or negative, like a fecal occult blood test. And that is a very important analysis. And I agree with it as being the primary analysis in many ways.

The point I was trying to make about the per polyp sensitivity is that that gets at the issue of --

and specificity as well -- the issue of when you're the gastroenterologist trying to find these lesions,

how does that impact your examination?

It could work either way, that you -- there's only a 12 millimeter lesion on the transverse colon, so that's all you're looking for, or it could be that you spend a long time looking for something that isn't there as Dr. Rex mentioned earlier.

DR. MC NEIL: Let's see, Bob?

DR. MC DONOUGH: I have a question for Dr. Zauber, just a quick question. When you were estimating the cost of colonoscopy, did you include the facility fee?

DR. ZAUBER: Our costs were the CMS costs for what CMS reimbursed. And so it has the -- it has the point of care charges. And so there's the facility fee and the physician fee. What we do not include was the copay and we also -- it's not societal costs. So the CMS cost there is the 80 percent that would have been reported.

DR. MC NEIL: Somebody else had a question?

DR. MOCK: I guess this question is for a couple of you in the front row. I have no doubt that

Dr. Klein can diagnose a polyp on CT colonography, and I have no doubt that Dr. Cash has a tight ship at the Naval Medical Hospital. And I enjoy listening to Dr. Cash, and I appreciate Dr. Patrick's comments.

I don't think, though, that Scottsdale is rural America. And as we talk about -- no. Rural America to me is Carefree, you know, it's Cottonwood, and it's Flagstaff.

You know, my concern is we sit up here on a panel and take responsibility to vote on an issue of this great importance. I'm anxious to have really any of you explain to me how this is something that you can feel comfortable that you can extrapolate from a quality perspective with measurable outcomes across not only the Midwest, but the rural areas in this country.

And if you have had challenges and you have experienced barriers in your centers of excellence, how is it going to go in that rural area where ten

20 percent of your primary care providers are doing your

21 endoscopy? I guess my concern is that one or a couple

of you can just reassure me and the others here that, as CMS represents all of our Medicare eligibles, and not just those in our metropolitan areas, how is this applicable across the country?

DR. KLEIN: That's a great question. I was almost going to say I'm not from a center of excellence, but that doesn't sound really good. I'm at an academic center. Okay? But it's an excellent question.

And the nice thing -- one of the opportunities I've had is to teach the American College of Radiology course to all the radiologists who want to learn this procedure. And they come from every small town you've talked about. Some are from Chicago. But some are from places in Minnesota where I go, where is that, and they go, you would never find it.

So it's a very, very excellent question. The nice thing about this procedure, whereas -- you

know, let's go back to colonoscopy for a minute.

There were several articles in the last

couple of years about the fact that not everybody performs the best optical colonoscopy, and some people can do these in twelve seconds, some people, it takes six minutes. The average, I think was eight minutes or some very small number. Clearly, that's a very operator-dependent procedure where you have some individual at one end of the scope who determines evidence found the whole way.

The nice thing about CT colonography is that these images are very reproducible, and they don't go away, and they can be reviewed again and again and again. And once you learn the technique to do it, the operator dependency drops.

You do need training. But I will tell you, from having trained a couple hundred people by now, I assume, something like that, people get very good at this, especially radiologists. And we have trained some gastroenterologists. But certainly radiologists who are used to interpreting CT scans get very good at

this.

Honestly, this is not brain surgery. So if

there's a neurosurgeon in the room, I admire you a lot more than I admire what I do. It's not that hard. It really isn't.

And I can train anybody at this table in a day or two days, how to do this, and you will be as good as the people that Dr. Fletcher and Dr. Johnson trained because if you're intelligent, educated, certainly if you're a physician experienced in some of this, you can learn how to do this. It is extremely, extremely reproducible.

And you should sleep very well tonight if you decide to approve this knowing that you are not turning loose, assuming you require some training, people who cannot master this. This is not that difficult. It is reproducible. The data is there to look at again the next day, if you want and the next day, if you want and the next day, if you want.

That's the comforting factor about CT colonography. And it should make -- I hope that

answers your question.

DR. MOCK: That's helpful. Thank you.

DR. CASH: I can speak a little bit to some of the things that we're doing as well. Not necessarily at -- well, it is at Bethesda. But we obviously serve a worldwide population.

One of the things that we've started doing now is we're doing teleradiology with our readers viewing the dichom images that are sent from remote hospitals, say over in Europe, Italy or Spain where they don't have somebody to do the colonoscopies. Real time, send us the CT images. They'll review them, and they spit it back at them with a reading within ten to fifteen minutes.

That's potentially doable. Obviously, it's going to take in these more rural settings -- and we were actually talking about this during the break -- was you know, what's the compliance rate with colon cancer screening in some of these rural settings?

The accessibility to colonoscopists, certainly gastroenterologists, is minimal in some of

these places. I think West Virginia has 30

gastroenterologists in the state. And then you've got

the whole quality issue.

So it is doable. There's a model there that maybe we'll able to set something up with regards to leading the way in terms of remote access. There are going to be issues with regards to same day colonoscopy in some of those models, especially in our European model, if you will.

But I think it will be doable, and I think the quality issue and the training will subsume a lot of the concerns about the quality if we do that the right way. And it needs to be done the right way.

DR. SINGH: This training issue in rural America is a very important issue. Even with optical colonoscopy, you know, which everybody said is the gold standard, in the last two or three years we've had multiple papers from community settings, different community settings.

Just from my own family, my younger brother published a paper in JAMA from Manitoba showing

perfectly (unintelligible) colonoscopies and ten year

after a negative colonoscopy, the incidence of colon

cancer is zero.

We did a study, my group did a study in California in the Medicaid population. Admittedly, not the most compliant, admittedly, not the ones who get the best (unintelligible), admittedly, not the highest reimbursement rates and spread over rural California. And we found our success rates were very close to what my brother published from Manitoba.

So even though the gold standard, there is a huge variation of what you find. So clearly with a new technology, one would seem as one would want to be assured that (unintelligible) is not there.

Not only 'cause you consider (unintelligible), but you are also introducing an equipment issue in here. At least for optical colonoscopists, the same optical colonoscope will (unintelligible), whether you have a gold-plated one or not.

But it's the same thing as we've seen for

20 years. Here we have an equipment related issue. I

21 don't know the technique well enough to know if

there's a technician related issue in it or not. And then clearly, it is the reader issue, too. So now there are few other variables in there. And I think one of the things that CMS would want to be assured of is that yes, in rural America it also works exactly the same way as it works in Dr. Cash's, the President's Hospital.

DR. BRILL: I would refer back to the fact that I think both the ACR and the AGA in their published standards have addressed some of the questions that you've addressed, Dr. Singh, regarding the technological standards and the like.

Dr. Mock, to your question, I'll get this wrong. Where's Doug? Dr. Rex was the lead author several years ago on a series that was published looking at quality standards in endoscopy. And the standards about what constitutes a quality colonoscopy was the subject of a task force convened under the AMA's physician consortium for performance improvement

which issued three measures on endoscopy and polyp surveillance earlier this year.

One of those measures was subsequently adopted by CMS as part of the 2009 PQRI measure set. The other two measures were adopted by the AQA Alliance at their meeting last month in October.

So we have processes in place, for example, on the colonoscopy standpoint, that address what should be a quality colonoscopy. With all due respect to Dr. Klein, it's not -- I don't think there are any 12 second colonoscopies being done these days.

But we have those standards. And I would assume that in a similar vein, we will have similar standards as have been mentioned for other types of procedures. I think what we're getting to is a very interesting point in our lives as physicians from a payment as well as from a practicing standpoint.

And that is that in the old days, it was I do, I bill, therefore I am. Okay? And I think nowadays, we're really getting to I provide a service, I measure what I do, I report on the outcomes. And we

use that information in order to say, I do a better job, or I don't do a better job.

And ultimately from a payment perspective, whether it is from a private commercial standpoint, whether it's from a government standpoint, we're going to evolve into that standard. We're going to have to unfortunately measure and rank and see what people do in order for us to make wise payment decisions.

DR. MC NEIL: I wonder if we're running short on time here. Did you have a quick comment on that?

UNKNOWN MALE VOICE: I was just going to address the technical quality.

DR. MC NEIL: Okay.

UNKNOWN MALE VOICE: And just briefly, I think that with 16 slice CT with automatic insufflaters, it's very easy to obtain a high quality exam. In the first five or seven years that we did CT colonography, we did a lot of these hand inflation, so the quality and the (unintelligible) was a much bigger problem. I think it's very easy to obtain a high

quality exam.

DR. MC NEIL: And they're pretty universally

employed?

UNKNOWN MALE VOICE: Fairly universally.

DR. MC NEIL: (Unintelligible.)

DR. SINGH: It's not a technician issue. Like you don't really -- there's not a technician variability as to who's doing it or the machine variability?

UNKNOWN MALE VOICE: I mean, obviously they'll need to be trained. They need to be able to read a scout CT to make sure that the colon is inflated, you know. But that's all part of the training. It's well laid out in the standards.

You have to understand how to use an insufflator. You know, you have to know how to run the CT scanner. But it's not -- it's not really rocket science. It can be done at a community hospital.

DR. PATRICK: The model that we're using we think is and can be very successful, whereby we

establish a radiology CTC hub. We're a spoke on the wheel, and we send by teleradiography in the States to

a CTC specialty hub where those, you know, specialists can make sure that they are meeting all the quality requirements, and we as gastroenterologists can feel that we have the same standards as followed in the ACRIN study.

DR. MC NEIL: One final question.

DR. PEARSON: It's a technical question. But we've talked a lot about interpretation. Can I just get clarity again? The question to us is about 16 slice scanners and above. My own personal communications with clinicians, at least the ones in metropolitan urban academic centers, they pooh-pooh anything lower than 64.

Can we just get a little bit of clarity because the data again that's in our systematic review, I believe, is predominantly or exclusively on 64 slice.

DR. JOHNSON: I don't think that's quite right.

DR. PEARSON: Okay.

DR. JOHNSON: The Pickhardt data was on 4

slice scanners. The National CT Colonography trial, the ACRIN trial, was on 16 slice scanners. So there weren't any of those that were on 64 slice scanners that I'm aware of.

Really, the only difference between 16 and 64 slice is just the data collection time. So the spatial resolution of the images, the collimation of the images, are all pretty much the same. The 64 just acquires it faster.

And since it's not like -- the colon is not like a beating heart, you don't really need to have a 64 slice scanner to do a really good job.

DR. MC NEIL: Any burning, emphasis on the burning, questions to the audience at this point?

DR. MOCK: I'm sorry. If I could just follow up? I thought I had this figured out, and now I'm really confused.

Dr. McFarland was talking about some data that came out of the study in Germany that made the

smaller polyp issue not a concern. And she's talking about different resolution in CT slices. And now,

you're -- I thought I just heard you say it doesn't matter if it's 16 or 64. The resolution is the same.

DR. JOHNSON: Beth, maybe you should come up, too. But the number of detectors is different than the collimation of the X-ray beam. You can have multiple detectors, and you can set those to -- you can set the collimation at different sizes.

So the ACRIN, that collimation was from .86 to 1.25 millimeters. You can set that same collimation on a 4 slice scanner or 16 slice scanner or a 64 slice scanner. So the spatial resolution therefore of 512 by 512 matrix is going to be identical whether you do it on any of those machines.

Again, the difference between those is just really the acquisition time of how fast you're going to acquire that data set.

DR. SINGH: So why can't you set up sensitivity that you can pick up a four millimeter polyp, for example? Can you set it up like that if

you wanted to?

DR. JOHNSON: Well, there are probably

limits. You know, if you take a look at the Pickhardt data that was actually at thicker collimation -- Beth, maybe you can remind me -- I think it was actually at five mills.

DR. MC FARLAND: It was at two-and-a-half.

DR. JOHNSON: Two-and-a-half? 2.5 millimeter data. ACRIN was 1 millimeter data on average. So you can see that the slice collimation and, therefore, the spatial resolution was better on the ACRIN data. But really, the performance wasn't any better.

DR. SINGH: Okay.

DR. JOHNSON: So there are limits --

DR. SINGH: To what you get.

DR. JOHNSON: You know, in theory, that would be true. In practice, it just didn't turn out that way.

DR. MOCK: Is there a cost discrepancy to be able to achieve that same result in the machine, the

equipment cost, the sum cost?

DR. JOHNSON: There's a cost in terms of

image noise or radiation dose. So as the collimation is narrowed, in order to get the same amount of signal, you have to increase the dose, or you have to be willing to live with a noisier image.

And so there's been a compromise. As collimation has gotten thinner, we've learned to live with noisier images. But there's also been some penalty in dose. But we talked about what the dose was with the ACRIN trial. And that represents a 50 percent dose reduction over standard body CT scan.

DR. MC NEIL: Is there anything you need to add to this?

DR. MC FARLAND: I was just going to say, the confusion was in the 64 row data of the Munich trial. That was -- the data was from five millimeter and greater was at that 90 percent. The other data at 16 row -- 4 row Pickhardt to 16 row ACRIN was six millimeter and greater, which averaged about 80 percent.

And always, it's the balance of you want to keep the dose low, but Dan just said, as you can see

smaller and smaller things, but you have to increase the dose to do it. And the issue of identifying more hypoplastic polyps and things that might not be worth going after. So it's setting that bar of the target lesion.

DR. SINGH: Well, like you said, you can't after see beyond a certain thing no matter what your resolution is. As you said, limits.

UNKNOWN MALE VOICE: There are limits set by technical (unintelligible). Now, you can probably see structures that are small as four millimeters for sure. (Unintelligible.) And little tiny bits of stool can also look like polyps.

DR. SINGH: Look like polyps.

UNKNOWN MALE VOICE: And hyperplastic polyps we don't want to (unintelligible). So you know, there's a compromising that we've kind of figured out where.

DR. MC NEIL: Jed, did you have a final

question?

DR. WEISSBERG: I had a different question.

I feel sorry for Dr. Calonge sitting here by himself. You talked about I, the insufficient. And I just want to ask, from the Task Force's point of view, your A ratings say do it. Figure out a way to get the service done. And your D rating or whatever say don't do it for sure.

Should the I rating be interpreted as a policy statement or a statement that you can't advise the policy makers?

DR. CALONGE: Ned Calonge with the Task Force. That's a policy question.

DR. WEISSBERG: Yes.

DR. CALONGE: So just to get back to the charge to the Task Force, which is to make recommendations, the I is not a recommendation. It's a statement. And we've actually worked really hard to turn it from a recommendation into a statement.

So my approach to an I from a policy standpoint could be -- I already know it's different

from a lot of people sitting on the front row, and it comes from a public health perspective. Anything you

do that increases the cost of care in the private insurance world translates in Colorado to increased people without insurance.

One percent increase in the costs of insurance care in Colorado translates to another 2500 Coloradans who don't have insurance. They become my problem in public health. So I see resources spent on insufficient data as a threat to covering other issues 'cause my pot is fixed, and I understand those issues.

So if you're asking me, I would say the I should translate to someone making a policy decision. But that's not the Task Force speaking. We only conclude we can't say.

And I would just say that's true of the positive recommendations. That when we gave the B recommendation to referring women for BRCA-1 and -2 counseling, I got a lot of calls that say, so does that mean we should pay for it? I say, no. That means we had sufficient evidence that we thought it

translated to at least a moderate health benefit.

And that's what the Task Force looks at.

Everything else becomes -- makes me an opinion person like everyone else. Sorry. Some of the people on the front row, and I won't say which ones.

DR. MC NEIL: Well, that was a loaded comment. Let's see. Did you have a very quick question?

DR. GOODMAN: Thank you. I shared among the panel --

DR. MC NEIL: Would you benefit from having --

DR. GOODMAN: As long as Ned was up.

DR. MC NEIL: As long as Ned is up, go for it.

DR. GOODMAN: Okay. So in the context of helping CMS make a better informed coverage decision, recognizing as we do and as you do perhaps better than anyone or at least in the room you do, there's an absence of evidence. We don't have enough evidence.

So can you tell us exactly, Ned -- Dr.

Calonge, what are the three most important evidence gaps that you would like to see filled that would move

the Task Force off an I? I have my suspicions based on what you and others said.

But if we had to force you to say what are the three chunks of evidence you need the most to move off an I to help CMS make an evidence-based coverage decision, what would those three evidence bits be?

DR. CALONGE: So to us the real -- and I hope that you did hear that the conclusion around sensitivity and specificity, at least for ten millimeters or more, which was what we were mainly considering, was okay. We were fine with that, and we could make the same link to health benefits associated with CT screening and we could for other non-visualization. So that part was okay.

So where the gaps came were all on the can we balance the other side and can we confidently and with certainty say the benefits -- sorry -- the harms are no more than small.

So the harms -- and there's only the two

gaps. The one harm was the harm of radiation. And I appreciate and I heard several times that the range of

the ACRIN study and the range that we've heard is lower than the ten millisieverts that we based our original conclusion on.

But they were also very close to that level, five to eight, five to nine. And I don't have a way to fill in that evidence gap.

DR. GOODMAN: The radiation is one.

DR. CALONGE: And the second is the potential risks and benefits of the extra-colonic findings. And so those are the two gaps that led us to say we cannot assign a harm that is no more than small with sufficient certainty to say that CT colonography leads to a net health benefit.

We were concerned that future research allowed for the possibility that those harms associated with the test itself and what comes from it could actually exceed the benefits associated with screening for colorectal cancer with CTC.

DR. GOODMAN: Okay. So you actually named

two, and those would push you off an I. Thank you.

DR. SINGH: I'd like to ask you one more

question. You mentioned that all this applied to polyps of ten or more. Were you also concerned about the lower sensitivity in six to nine, and the possibility of missed polyps less than six? Did that come into your considerations?

DR. CALONGE: As you recognize in the evidence report and even in our recommendation statement, we did talk about smaller polyps, six to nine millimeters, and that we felt the data were inconsistent.

And that inconsistency leads to another level of uncertainty. I think again we felt pretty confident that if you set the cut-off at ten, we could translate that to a health benefit equivalent to that of other tests. And so that's where we're comfortable.

But there is controversy. I mean, again, we have trouble with people saying that everything's better now. And the problem we have with that is we

actually don't have comparable studies that say

everything is better now.

We had the same problem with mammography. Ignore the Canadian study. Old stuff, doesn't work, it was a bad study. And we say, well show me new data. Well, we're not doing new data 'cause we already showed it worked.

So we get stuck with this it's all better now. So I think what I would conclude from the overall analysis of the data, looking at admittedly slightly older studies -- I mean, we're not talking 80s, we're talking 2000 -- older studies and newer studies that there is some inconsistency in the sensitivity around the smaller polyps.

DR. SINGH: And from the public health perspective, you will really want the smaller polyps?

DR. CALONGE: Yeah. I think that concern about the natural history of the small polyps, especially in your age group, which are things that I actually learned sitting here today, are things that, if I was sitting there, which I'm not, I would have to

kind of pull into consideration.

Is there a faster time frame? I don't know.

What's the natural history of these smaller polyps? And if we're missing them or not following up on them or using additional tests to follow them over time, what's the net health benefit associated with detecting those or not detecting those?

DR. SINGH: So then your concern of the I would be, you said in greater than ten, your two concerns were related to the safety issues. But in six to nine, your third concern in that I recommendation would also be on the benefit side, not just on the harm side, but on the benefit side.

DR. CALONGE: And the way I would look at that is that it brings in another issue of uncertainty. But I would be ingenuous in talking to you if I didn't say that the big concerns were really on the harm side.

DR. SINGH: Okay.

DR. MC NEIL: Let's see. Did --

DR. MC DONOUGH: I have a question for Ned.

DR. MC NEIL: Quick.

DR. MC DONOUGH: So the I recommendation or

any of the recommendations from the Task Force is not a recommendation for coverage. I know CMS is concerned about being consistent with the U.S. Preventive Services Task Force. Is it that a positive coverage recommendation for CT colonography, would that be inconsistent with the Preventive Task Force recommendations for CTC?

DR. CALONGE: Well, you know, that's a really great question. And the way I would answer that is that people make recommendations and actually assign practices all the time that go beyond what the Task Force recommends. I will tell you they do it for different reasons, usually, contextual reasons.

And I think -- from my value based, there are good contextual bases. I think it might work. It might increase screening. I can actually see some benefits in this area.

And there are bad contextual issues from my standpoint. I can make money on it. I can generate a

new revenue center or some other benefits that may be not accruing to the overall health of the population.

So I think you can look at it both ways. And people do that all the time.

Your question is whether or not that's inconsistent. What I would say is that we would say that it's not evidence-based using our methods. And someone said, wouldn't you agree that the bar set by the Task Force is pretty high. I would say I would agree with that.

What that translates to is a set of recommendations that I can look at everyone at the table and say, if you did the A's and B's, I guarantee you you would improve the longevity and health of the population. If you did the C's, I'm not so sure. If you did the D's you're wasting money, and if you did the I's, you may be facing a study that comes along and disproves it some time in the future.

The other thing I would -- the last thing I would point out is that coverage decisions that precede the evidence make it very difficult to

20 actually get the evidence.

21 DR. SINGH: Correct. That's very, very

important.

DR. MC NEIL: Let's see. Okay.

DR. PEDEN: I just want to ask Dr. Goodman's question a different way. And I think it's Dr. Singh's question a different way, too.

He had asked what were the two or three things that would get you off of an I, and you focused on the harms perspective. I think Dr. Singh identified maybe one of the benefits perspective.

Can you think of other benefits perspective that might weigh that net equation to get you off the I, or are there no other things other than the confidence between six and nine? I'm thinking things like increasing the rate of screening and things like that.

DR. CALONGE: So the issue about whether or not we improve penetrance into the population is a good issue. It really comes at the issue of, at what expense?

So if we're achieving better colorectal cancer screening because we added another choice that

people want and that we would expect to get the same mortality reduction from colorectal cancer, if that's at the expense of some additional harms, so you gain adherence, you get more -- you know, you win the colorectal cancer battle, but you lose the life war.

Then that would make it very difficult for us to say that's a health endpoint into itself without answering the harm issue. I am intrigued by the issue that it could increase screening. So if we had that in context of, God forbid, an actual reduction in colorectal cancer mortality in the population, then there could be other evidence things that help -- come in that would make us feel a little bit stronger about the -- might be able to move us off the insufficient evidence issue.

And this issue about efficacy versus effectiveness was your question. And it really varies by the task. It took us twelve years before we could confidently assign a reduction in breast cancer

mortality to mammography. And then the DAMES (phonetic) looked at it at ten years, they saw no

benefit. And that's what generated the Grotschy and Olsen (phonetic) review that says it's not effective. So if they had waited another couple of years, maybe they would have seen that.

This issue about what our endpoint is, which is making people live longer and healthier, not necessarily changing what they die of, that's something I think you have to keep in mind from a policy standpoint.

DR. MC NEIL: Let me ask the group a question. What do you want to do?

DR. KLEIN: (Unintelligible) talked about?

DR. MC NEIL: No. Not yet. If it's one second. I'm really concerned. I want to have everybody vote.

DR. KLEIN: We just talked for 15 minutes about this, and it's -- some of the things are just not accurate. So I think it's only fair.

DR. MC NEIL: Well, tell us the errors.

Tell us the errors.

DR. KLEIN: Really quickly. The two points

-- you brought up a great question, Dr. Goodman. And that is what two things would move you off. First of all, I know you didn't mean to insult those of us in the front row, so we forgive you. Don't worry about it.

But the two things you said, one, extra-colonic findings. This is not -- this is not unknown. The Pickhardt study from 2004, Dr. Cash's data, those of us who have done thousands of these will tell you the incidence of significant extra-colonic findings is about four percent. So I don't know why that's still an issue on your plate, but it's not on mine. And anybody who does a lot of these, it's not. So that's not accurate.

Number two, radiation. Again, 65 and older, the risk of radiation here, even if you believe the BEIR report, and, of course, we'll never have an answer to this in our lifetime. The risk to 65 and older, I think all of us who have been dealing in

radiation for years and years and years and years will

tell you, this is a non-event.

If you want to stop screening at 75, maybe they'll have two scans. It's irrelevant. It's not going to affect anybody negatively. But the benefit of finding those cancers is huge.

So I disagree with you. I don't see why you can't move off your I 'cause those two issues, as far as I'm concerned, and many other people -- and the data support this, not just my opinion, the data support this -- is that those are not issues. And you should be able to feel free to move right off those and take that I back and give us a favorable review if that's your only concern.

DR. MC NEIL: Thank you. Steve just raised the issue to be clear about the radiation. It's a cumulative effect. So you would be adding on ten or twelve millisieverts to whatever they've had up to age 65, or 25 if they had a couple. It wouldn't be a one-shot deal.

But let me ask, just before anybody raises

their hand, what do we want to do at this point?

Several people -- well, at least two people -- three

people are leaving. And I do want to make sure as many of us vote as possible. So what would the group like to do?

We have two options. One is we can continue this dialogue with the panel -- with the audience and the people who spoke, or we can talk among ourselves, realizing that whatever we do, in 45 minutes we vote.

DR. SINGH: I think we should talk among ourselves specific to the questions that we have.

DR. MC NEIL: Okay.

DR. SINGH: We could pick up the issues and start talking, and then maybe even work on the questions as we continue talking. We accomplish two things at once.

DR. MC NEIL: Does that meet everybody's pleasure? Cliff?

DR. GOODMAN: I'm not sure how we would proceed. Can you just clarify? Do we just go question by question?

DR. MC NEIL: One thing I think Dr. Singh was suggesting, that there are two ways we can do it.

One is we can say we still have a number of random burning questions that we can talk to ourselves about. And they may or may not generate a question to the audience. Or we could focus those questions and doubts we have in the context of the questions that we need to answer.

DR. SINGH: That's what I meant, the second.

DR. MC NEIL: And I think he meant the second. We could obviously do the first and say, you know, what's the radiation dose really likely to be in 2020? I mean, just picking a random irrelevant question for these sets of questions.

But we could do either. So I hear -- what's the preference? We're not ready to vote.

UNKNOWN MALE VOICE: Work through the questions.

UNKNOWN MALE VOICE: I vote for number two.

UNKNOWN MALE VOICE: I vote for number two as well.

DR. MC NEIL: You vote for?

DR. SINGH: Number two.

DR. MC NEIL: You focus laser-like, precise, go for the questions.

UNKNOWN MALE VOICE: Let's go to the questions.

DR. MC NEIL: So let's just look at the questions. And you can all read them. I'm not going to read them. So then we rate the sensitivity and specificity for polyps of varying sizes for an average risk individual. And we've not specified anything more than an average risk individual.

So we need to discuss among ourselves any comments we have or concerns or questions about sensitivity and specificity. And that's independent of benefits. This is pure, hard core -- yes. Steve?

DR. PEARSON: One comment is just, to a certain extent, the sensitivity and specificity for polyps less than six millimeters is kind of not applicable because it really hasn't been looked at or considered to be reportable in most studies. So I

don't think --

DR. PHURROUGH: The question is, is there

evidence.

DR. PEARSON: Okay.

DR. PHURROUGH: It may not be applicable in the second question.

DR. SINGH: So then it is no confidence.

DR. PEARSON: Little confidence.

DR. SINGH: You have little confidence in the evidence 'cause it doesn't exist. So that is the easiest question.

DR. MC NEIL: That's an easy one. I did that one without --

DR. PHURROUGH: Let me emphasize the questions -- we had this discussion in our phone call earlier. The first question -- the first two questions is is there evidence. The first one is there evidence on the test characteristics, the second one is there evidence on health benefits. And then we start getting to how do you apply that evidence. So we focus on quantity and quality of evidence on these

first two questions.

DR. MC NEIL: Okay. We got rid of 1-A

pretty easily. At least, I think.

DR. SINGH: So you want us to shuffle the cards?

DR. MC NEIL: No. I think what we're going to do, Dr. Singh, is we'll -- we all may not come with the same number. So let's discuss it, and we'll right down something on our own piece of paper. And then that actually may be changed by the time we get to question seven. If you like, I suppose we could vote as we go along.

DR. SINGH: I suggest that we vote as we go along. Then, you know, people who are way outliers can get a chance to explain why they think the way they do.

DR. MC NEIL: Defend themselves?

DR. SINGH: That's how I've done it when I sat at FDA committees. We go along, and people who are way outliers then get a chance to explain that. And some votes change as we go along.

DR. MC NEIL: So are you saying that we should discuss question one, all three parts --

DR. SINGH: Right.

DR. MC NEIL: -- and then vote.

DR. SINGH: Vote. And then go on to question two, and then so as we do the discussion, we also continue voting. So by the 45 minutes or one hour, we're done with everything.

DR. MC NEIL: How do people feel about that?

DR. GOODMAN: How does Dr. Phurrough feel about that?

DR. SINGH: Yes.

DR. PHURROUGH: Oh, I'm --

DR. GOODMAN: Have you seen it work either way, Steve?

DR. PHURROUGH: When I comes to the voting time, I'm a bystander. I'm more than happy -- I have no trouble with you doing it that way.

DR. MORRIS: One thing I'd like to suggest that we've done at the National (unintelligible) on occasion is at the very end ask if anybody would like

to -- just go back through one more time and ask if anybody would like to change their vote based on the

subsequent discussion.

DR. MC NEIL: Can we do that, Maria?

MS. ELLIS: That would be fine as long as you show it on your score sheets because at the end, we'll collect them to make sure we have all the correct scores. It's inside your yellow or green folder. You should have a score sheet with each one.

DR. MC NEIL: Do you have any extra score sheets?

MS. ELLIS: Do you need one?

DR. MC NEIL: Yes. Oh, here it is. Okay, everybody. Here we are.

All right. So I think we dispensed with the polyps less than six millimeters. How do we feel about the data on --

DR. SINGH: Less than six millimeters --

UNKNOWN MALE VOICE: Are we voting?

DR. MC NEIL: No. Let's do all three first. All right. Let's do polyps less than six, six to ten,

and greater than ten, and then we'll go back and vote

because it might be a little bit of movement depending

upon -- is that okay?

UNKNOWN MALE VOICE: Okay.

DR. MC NEIL: Let's finish the discussion, though, on less than six. So now let's go on to the discussion of six to ten. How do people feel about that? Do they have any questions of the audience, the speakers, questions of each other?

DR. MC DONOUGH: I have a question for you. Do you think that your question about how getting information, how it was calculated or estimated in the cost-effectiveness analysis for estimating sensitivity and specificity for six to nine was adequately answered?

DR. MC NEIL: Well, I didn't get it. But I may have been slow, to be honest. I didn't understand it.

UNKNOWN VOICE: You did or you did not?

DR. MC NEIL: I did not.

DR. SINGH: So basically it's this slide

we're talking about. How did you get the information in the middle of it, the six to nine millimeters.

DR. MC NEIL: Yes. I didn't understand where that came from.

DR. SINGH: This slide.

DR. MC NEIL: Right. Yes. You can tell us. That would be great.

UNKNOWN MALE VOICE: Ann, I think your explanation before was that it was mathematically derived, that it's not based on actual evidence from the report. Correct?

DR. ZAUBER: From the people who (unintelligible) adenoma table and a patient table. We took the adenoma table, and you've got greater than or equal to six, and then you've got greater than or equal to ten. So the six to nines are in between. So you take your numerator and your denominator, you take the --

DR. MC NEIL: So you knew the numerator and the denominator 'cause that's not --

DR. ZAUBER: Pardon?

DR. MC NEIL: You knew the numerator --

DR. ZAUBER: It's in the actual paper in the

New England Journal, the two papers.

DR. MC NEIL: Oh, but it's not here. Okay.

UNKNOWN MALE VOICE: (Unintelligible.)

DR. ZAUBER: No. What? No. It's not.

UNKNOWN MALE VOICE: You're showing me a picture which I can't --

DR. SINGH: No, no, no. But those numbers are not in the New England Journal of Medicine paper.

DR. ZAUBER: The subtraction (unintelligible).

UNKNOWN MALE VOICE: So it's a derivative. It's a mathematical derivative. It's not real data.

UNKNOWN MALE VOICE: I'm not sure we want to get into the weeds on this.

DR. MC NEIL: We may not want to get --

DR. PEARSON: There are three papers that our systematic review found that did have specific per patient sensitivity and specificity for six to nine millimeter lesions. Johnson 2007, Rocky (phonetic)

2005, and Taylor (phonetic) 2003.

DR. SINGH: But you need a per polyp.

DR. PEARSON: Pardon?

DR. SINGH: You need a per polyp sensitivity and specificity?

DR. PEARSON: Right. I don't have -- we looked at it as per patient. That's why --

DR. SINGH: Correct. That's why I was wondering how they get the per polyp one here.

DR. MC NEIL: That was my question. You're right.

DR. SINGH: Yes. We have the same question.

DR. MC DONOUGH: One other sort of comment also that I have, it seems like there's greater variability between Pickhardt and ACRIN in terms of those calculations for six to nine then -- or greater than six then greater than ten.

In other words, less consistency which might translate into less certainty.

DR. SINGH: Exactly.

UNKNOWN MALE VOICE: Yes.

DR. SINGH: Exactly. That's also my point.

DR. MC NEIL: So all right. So no more

comments on this, then. We don't really know the per adenoma sensitivity and specificity, or at least we don't think we do for six to ten. Is that right? Six to less than ten.

DR. MC DONOUGH: Less, certainly in my opinion.

UNKNOWN MALE VOICE: Less.

DR. MC NEIL: Less. Okay. Well, why don't we move on to greater than --

DR. SINGH: The (unintelligible) the study is here. That's data that should be obtainable. Right? If we ask you for that data, that should be obtainable. Isn't it?

DR. MC NEIL: I thought I looked, and I couldn't find it before we came down. But I didn't bring the paper with me.

DR. SINGH: I know. But we have the principal investigator of the study here.

DR. MC NEIL: Well, that's better than the

paper.

DR. JOHNSON: Well, I don't think it is

'cause I don't remember those exact numbers. We could get it for you.

DR. SINGH: You could get it for us.

DR. JOHNSON: The reason it's reported this way is this is how we manage patients. Okay? I mean, you don't manage a six to nine millimeter polyp, you manage a patient. Do they have a six millimeter polyp or larger, and how are you going to treat that patient? Do you send him to colonoscopy or not?

DR. SINGH: We understand.

DR. JOHNSON: So we reported this because this is how it should be used.

DR. SINGH: Our question is framed in a slightly different way. We're trying to answer our question on the way you reported the data. And they don't quite synch. That's the only issue.

DR. MC NEIL: Maybe I'll make a suggestion here, if you would let me? I would make a suggestion if Steve will let me. He's looking doubtful.

That we answer question B and that we put in a question B-2 which is six to greater than ten -- or

greater than or equal to ten. Will you let me do that?

DR. SINGH: Or greater than or equal to six.

UNKNOWN MALE VOICE: Greater than six.

DR. SINGH: Greater than or equal to six you mean.

DR. MC NEIL: I mean -- sorry -- greater than or equal to six. So let's think about 1B, six to less than ten. And let's focus -- think our thoughts and write something down tentatively.

Now, we have another little question in there that's greater than or equal to six, and then the C is greater than or equal to ten. Is that okay? Does that make sense? Thank you, Bob, for that.

All right. So let's do the greater than or equal to ten first 'cause that's easiest. Do people have any questions about -- among each other or with the panelists or anybody in the audience about the sensitivity and specificity of greater than or equal

to ten millimeters per adenoma?

Are you ready to vote? All right. How

about for the greater than or equal to six?

DR. SINGH: Greater -- less than or equal to six, you mean?

UNKNOWN MALE VOICE: Are we voting?

DR. MC NEIL: No. We're writing them out. We're writing on our paper. I'm sorry. We're not voting yet. Am I confusing everybody here?

DR. MC DONOUGH: Obviously, greater than or equal to six, we would have more confidence if we had the data.

UNKNOWN MALE VOICE: Right.

DR. SINGH: So we called it one.

UNKNOWN MALE VOICE: One or two.

DR. MC NEIL: Okay.

DR. SINGH: So we did already vote question 1-A?

DR. MC NEIL: We did 1-A, 1-B, 1-B-2, and 1-C.

DR. SINGH: But we're going to do the voting

now, right, on those?

DR. MC NEIL: So the voting is the same

except for 1-B-2 is polyps greater than or equal to six.

DR. SINGH: Correct. Okay.

DR. MC NEIL: This is a little confusing. Is everybody --

DR. SINGH: No, no, no. We're saying are we ready to vote now. Should we start voting?

DR. MC NEIL: No. Any second I'm going to ask you to hold up your hand.

DR. SINGH: Okay.

DR. MC NEIL: Any second. Live in hope. Live in hope.

DR. SINGH: I'm just itching to vote.

DR. MC NEIL: You're dying to hold up that number one. I can tell.

UNKNOWN MALE VOICE: You didn't have enough voting a couple weeks ago?

DR. SINGH: I was out of the country, actually.

DR. MC NEIL: Is everybody ready here?

DR. ZAUBER: We think that perhaps in your

paper you mean polyps or adenomas in the second table because that adds up to another table that you have. So that looks like you have that.

And if you look at the Pickhardt table, you have 180 adenomas detected out of 210 of size greater than or equal to six, and you have 47 adenomas detected out of 51 detected, and you make the subtraction in the numerators and the denominators, and you come up with exactly the figure we have.

So we're taking it from table three of the Pickhardt paper where it has 180 over 210, and you've got 47 out of 51 over those adenomas greater than ten millimeters. So it's a straight subtraction of the numerators at risk of the adenomas detected and over those that were detected by optical colonoscopy. So it's a straight derivation.

DR. MC NEIL: From one paper?

DR. ZAUBER: This is from Pickhardt. And the same thing would be true of the ACRIN 6664. The

only thing is that the denominator is stated in the paper. It says it's patients, but it matches to the

previous table for adenomas.

DR. MC NEIL: Oh. Okay.

DR. ZAUBER: But that's where it's coming from. And we had done the calculations from our models, all three models doing it for per patient basis and per adenoma basis, and we get comparable effects.

DR. MC NEIL: Well, that's not the question, though.

DR. ZAUBER: No. But I'm telling you that our definitions or our use of the sensitivity per adenoma categorized or whether it's categorized as the sensitivity of adenomas on the patient point of view does not change the results that we get. It's just the way we model it. It's easier per adenoma for us.

DR. MC NEIL: Okay. Great. Thanks.

All right. We're going to hold up for 1-A. Is that right, Maria?

MS. ELLIS: Please hold up your cards.

(Whereupon, the panel voted.)

DR. MC NEIL: 1-B, six to less than ten.

(Whereupon, the panel voted.)

DR. MC NEIL: 1-B-2, greater than or equal to six.

(Whereupon, the panel voted.)

DR. MC NEIL: Greater than or equal to ten.

(Whereupon, the panel voted.)

DR. PHURROUGH: Just to remind the panelists, please make sure you're marking these numbers on your score sheet 'cause you're score sheet is official. These cards are for public consumption. The score sheet is official.

DR. MC NEIL: Do we need them notarized.

MS. ELLIS: I'm sorry. I apologize. For the record, it was inadvertently omitted, Dr. Steve Pearson is a voting member.

DR. MC NEIL: So I'm fake. Right?

MS. ELLIS: No, Barbara. You are not fake.

UNKNOWN MALE VOICE: She's extraneous.

DR. MC NEIL: Okay. I'm extraneous. I'm

extraneous. Okay. Barbara's extraneous.

DR. PEDEN: Dr. Phurrough, with the addition

of the additional question, how do you want us to deal with that on the official card?

DR. SINGH: Write it in. Write it in.

DR. PEDEN: Okay.

DR. MC NEIL: Just stick it in. They'll figure it out.

So we're going to add that same question to number two as well. Right?

DR. MORRIS: So just to clarify, number two is going to have two part B's. Is that what you're saying?

DR. MC NEIL: Yes. Same thing. Exactly.

So let's talk about benefits. I'm sorry.

DR. SINGH: Question two, the way I read this question is how confident are you that there's sufficient evidence to determine the health benefits. And the way I interpret health benefits is as the U.S. Task Force did, like net health benefits. Is that --

DR. PHURROUGH: Yes.

DR. SINGH: -- correct?

DR. PHURROUGH: Yes.

DR. SINGH: So is there a net health benefit, like how do you save lives. And that's obviously a difficult metric to meet because net health benefits are not shown in any of the clinical trials. You know, we talk about modality, we talk about life-years saved, we talk about cancers prevented in the community. None of the studies show that. At least, I can't see that.

DR. MOCK: To be fair, I want to be clear. That word net changes the nature of the question --

DR. MC NEIL: Completely.

DR. MOCK: -- completely. If it's supposed to say net, we should write in net.

DR. MC NEIL: We should write in net.

DR. MOCK: And we should make the distinction that it's net.

DR. MC NEIL: Correct. That's what I was going to recommend. Exactly. Write in the word net so that there's no question about the question you are

answering.

DR. SINGH: Of course, health benefits is as

we interpret it, or I interpret health benefits as life-years -- you know, colon cancer avoided, not polyps detected.

DR. MC NEIL: Correct.

DR. SINGH: 'Cause we know that there is a lot of, you know, slip between the cup and the lip where polyps detected is hundred percent and cancers prevented is much less than that.

DR. MC NEIL: Right. That's the reason for separate questions one and two. Exactly right, Dr. Singh. Okay.

DR. PEARSON: I just wanted to -- the other key issue here for framing is in some people's mind, they'll be comparing that net health benefit to no screening and others to a patient who could alternatively be screened by optical colonoscopy.

And so I just think we ought to be clear about whether we are judging --

UNKNOWN MALE VOICE: It says compared to

optical colonoscopy.

DR. PEARSON: -- the net benefit explicitly

as compared to --

DR. SINGH: It says compared to optical colonoscopy.

DR. PEARSON: It is in there. Sorry. That's good that I clarified that for myself.

DR. MC NEIL: So let's just talk now about net health benefits for these various sizes. How do we feel? Yes, Michael?

MR. LACEY: We haven't explicitly talked about optical colonoscopy, what the evidence is or what the net health benefit is of optical colonoscopy 'cause my understanding from the reading was fecal occult blood testing was the only one that had done a -- you know, a trial that led directly to a reduction in mortality. And the benefit of optical colonoscopy was under the assumption that removing polyps would also have that.

So to me, if we can feel confident that CTC works as well as optical colonoscopy, then you just

leap over to the same conclusion, that optical

colonoscopy has a benefit, which I think everybody

obviously thinks it does.

DR. TEUTSCH: We had a long debate about this on the Preventive Services Task Force. But the -- and I should let Ned comment more. But what we basically said, FOBT doesn't work because you get the FOBT. It only works because you get the polyps out. Colonoscopy is the definitive treatment. Clearly, it must be effective.

And so we basically accepted that as -- since it was the gold standard. And then the question is, to what extent do you get those same polyps out using other modalities.

DR. MC NEIL: Dr. Singh, did you want to comment?

DR. SINGH: Yes. I was going to say that I'm not sure whether one could assume that if you have the same polyp detection rate, say, for -- but if you had the same exact polyp detection rate for every size polyp, yes, you could probably assume it.

But there's something else that colonoscopy does. When a gastroenterologist goes in, he sees that

three millimeter polyp, he removes it. He doesn't let it be there. He sees a two millimeter polyp, he removes it. So he removes everything as he is going through, and he cleans the colon.

So one can't say that another technique that's not up with CTC, but say some other gold standard technique, that detects all the polyps, but only removes the ones that are more than six millimeters will have exactly the same health benefits as a procedure that goes in and completely cleans the colon. 'Cause I think that assumption is not an easy one.

And in the second question I wanted to answer, what are the net benefits of colonoscopy, have they been shown? They have been shown. There have been multiple studies that -- the ones on extending life are more controversial.

The ones on prevention of colorectal cancer are definitely there. There are -- there was a case

controlled study from Kaiser Permanente. There was a long-term cohort study that my younger brother

published from Manitoba that over a period of ten years when compared to a group that was not screened, patients in the colonoscopy group over ten years developed no new cancers.

We didn't find the same efficacy in the Medicaid population. So my data, which is right now in press at (unintelligible) Medicine, we've found about a 50 percent benefit. So compared to patients who were not screened compared to patients who were screened, at the end of five years, the colonoscopy group had a 50 percent reduction in colorectal cancer -- in (unintelligible) colorectal cancer compared to patients who were not screened.

But that's how colonoscopy is done in the community. That's what I was pointing out. It should be a hundred percent, but we didn't see a hundred percent. So that is demonstrated. So for colonoscopy, the health benefit is demonstrated, and there's evidence.

MR. LACEY: Right. And I --

DR. SINGH: I'm not just assuming.

MR. LACEY: Well, that's why I just wanted to have the discussion because that wasn't part of the reading.

DR. SINGH: Sure. Exactly.

MR. LACEY: (Unintelligible) for the very small polyps, it's my understanding, most of them do not progress, or if they do progress, they progress over a ten year period, which you would catch in the next screen. So whether you remove the very small ones, whether that leads to a net health is controversial.

DR. SINGH: They have to show it, you know. That's the idea. They have to show it, that not removing it doesn't harm you.

MR. LACEY: Yes. I guess I was just making sure that if we felt that the technical performance characteristics of CTC, you find the polyps, and the assumption is you remove them with optical. Why would you not be able to assume that that, in fact, is

exactly the same net health benefit as what you get

with optical colonoscopy?

DR. SINGH: 'Cause, A, you only remove the ones over six millimeter, and B, you wouldn't even find all the ones that were six millimeter. So there are two gaps there. So you could assume that those are the only ones that make a difference. But that's an assumption. I think we are (unintelligible) here what is the evidence. And the evidence isn't there. Not yet.

DR. WEISSBERG: Dr. Singh, your point is correct in concept. But I would just point out that from my perspective, I'm not sure we're actually doing people a lot of benefit when we're removing two and three and maybe even four and five millimeter polyps. They're being subjected to the risk of polypectomy.

We should remember that in the future, actually in the near future, there will be optical biopsy, quote, unquote, "techniques," to decide whether or not we really even need to bother with some of these little polyps.

And we should weight our attention, I think, in conjunction with the evidence of, you know, the

size of polyps related to the risk of malignancy. So that would lead you to be much more concerned about the larger polyps.

DR. SINGH: That's --

DR. PHURROUGH: Just to make a comment about the question itself. In formatting this question, there's sort of -- there's a framework to keep in mind. We are comparing it to optical colonoscopy, so there is a legitimate question as we've been discussing, what are the health benefits of optical colonoscopy, looking at both benefits and risk to get to that net question.

For CTC to realize health benefits, you have to make the leap from getting those polyps that have been identified at CTC into the treatment realm of optical colonoscopy. So there's this question of adherence. So adherence is a real evidentiary question here in this question. Is there evidence that you can get those polyps that you see at CTC into

20 OC?

21 And then you have to take into account, you

know, the false negatives. You get more CTCs, and you're exposed to more risk. And the savings from a benefit point of view, the increased benefit of not sending those who don't have polyps to OC where they, in fact, would have potentially higher harms, assuming a high sensitivity and not worried about the false positives on that side.

So all of those are wrapped into this particular question that have to be considered. Do we have evidence of all of that?

DR. SINGH: I wanted to just share some more data with you because the benefit of colonoscopy, you know, came up. Some further data from our community study in Medicaid, which is, as I said, presumably the worst population to look at from multiple different reasons. So that's the worst case scenario one would think of when we have benefits of colonoscopy.

So almost about a 50 percent benefit overall. And left-sided CRC, colonoscopy was very,

very good. Almost 84, 85 percent reduction in

colorectal cancer. It's on the right-sided colorectal

cancers that we had a problem.

And that's something CTC may have an advantage over 'cause the right side of the colon, especially in the community colonoscopy setting, patients -- you know, doctors want to go in and come out very quickly. Medicaid doesn't pay very much, so why spend so much time on it? I mean, I don't know.

There now your benefit is only about 33 percent. And as well, as we found a difference between men and women. Men tended to do a lot better than women. And women on the right-sided tumors, the health benefits were not very much, at least in our study. And that also is consistent with previous data, that women tend to have more incomplete colonoscopies, and it's generally a more difficult anatomy.

DR. MC NEIL: Steve?

DR. TEUTSCH: Just one thing to add to what Steve Phurrough said. The other part is the

confidence we have in the harms associated with

whether the radiation causes cancer, and particularly

the harms or benefits associated with the extra-colonic finding because it seems to me that fits right into the net benefits, in addition to the ones that Steve mentioned.

DR. MC NEIL: So let's see. Jonathan?

DR. WEINER: Barbara, quick question.

DR. MC NEIL: I'm sorry. Who was that?

DR. WEINER: I'm speaking about number four. Now we've added net benefits. Four includes net benefits. Granted, it adds the word Medicare. But then the footnotes talks about the issue that Steve just mentioned.

So clarification, the difference between two and four?

DR. PHURROUGH: Two is, is there evidence. Four is, what does the evidence show.

DR. SINGH: Exactly. Two is, is there evidence.

DR. WEINER: Oh, is there evidence. We

don't care what it is. And then --

DR. SINGH: What is it. Yes.

UNKNOWN MALE VOICE: Can you draw a conclusion?

DR. PHURROUGH: Is there sufficient evidence to arrive at a conclusion that's asked for in question four?

DR. WEINER: Okay. So we keep those two issues separate.

DR. SINGH: Because if there is no evidence, then you cannot answer that question.

DR. MORRIS: So the thing that I'd like to point out is that as Curtis said, really when we're talking about net health benefits, it's a very different game. For polyps that are less than six millimeters, the chance that the polyp contains a cancer is very tiny.

But colonoscopy -- for comparing to colonoscopy, it's the only screening test that has a mortality rate. Virtual colonoscopy doesn't really have a mortality rate. I'm saying that's something to

keep in mind. It would really change our answer to 2-

A.

DR. MC DONOUGH: A question about that. Can you have any confidence in your answer to 2-A if you answered 1-A that, you know, that you have no confidence. I mean, if you don't know the test characteristics --

DR. MORRIS: We're talking about harms. We're talking about harms.

DR. MC DONOUGH: That there's sufficient --

DR. MC NEIL: Well, if one is one, can you go below one I think is what you're asking. Right?

DR. MC DONOUGH: Because I understand what you're saying. I mean, we're very confident that there's little benefit -- or more confidence that there's little benefit in removing polyps that are less than six millimeters. But on the other hand, we don't have any confidence that CTC can even detect them reliably.

But maybe that's -- I think what you're saying, that they're irrelevant because you don't want

to remove them anyway.

DR. MORRIS: Well, basically yes. And

because you won't die.

DR. MC DONOUGH: Yeah. I see.

DR. MC NEIL: Everybody got this one? Okay. Shall we vote? So we're looking at sufficient evidence on net health benefits. Got it? For less than six millimeters.

(Whereupon, the panel voted.)

Could we ask for a clarification? I wanted to make sure you were answering the same question. Just glancing at the numbers, you're an outlier.

DR. MC DONOUGH: Maybe we're thinking the same thing.

DR. MORRIS: I think that the presence of a polyp less than six millimeters is not very meaningful. But that the risk of colonoscopy -- the risk of mortality with colonoscopy actually exists, whereas with CTC -- I'm sorry. What did I say? The risk of mortality exists with colonoscopy, but it doesn't exist with CTC for a polyp of that size.

So if we're talking about numerators and denominators, in this case --

DR. SINGH: I wouldn't say that it doesn't exist.

DR. SINGH: I wouldn't say that it doesn't exist. Look, the benefit of CTC is not in CTC itself. The benefit of CTC, CTC followed by colonoscopy. So if you give the benefit of the second colonoscopy to CTC, why don't you give it to --

DR. MORRIS: Because folks wouldn't have a second colonoscopy. They wouldn't have a colonoscopy.

DR. SINGH: No. What I'm saying is, for the CTC -- what you're comparing is not CTC versus colonoscopy. You're comparing CTC followed by colonoscopy with colonoscopy.

DR. MORRIS: No. I'm comparing -- no. The question is for polyps less than six millimeters. So these patients would not go on to a colonoscopy.

DR. SINGH: Oh, okay. That's what you mean.

DR. MOCK: I'm sorry. I'm confused. I thought this question was asking about whether there

is sufficient evidence.

DR. MC NEIL: It is.

DR. SINGH: Yes.

UNKNOWN MALE VOICE: I agree with Arden a hundred percent. But I didn't think that was what was being asked in the question.

UNKNOWN MALE VOICE: Exactly.

DR. SINGH: Right. Is there evidence? Is it proven?

DR. MORRIS: Right. There's evidence of mortality with colonoscopy, with screening colonoscopy.

UNKNOWN MALE VOICE: That's just one part of it.

DR. MC NEIL: So I guess --

DR. SINGH: But it also has benefits, you know. Is there health benefits there?

DR. MC NEIL: I guess one of the questions -- maybe we need Steve to weigh in on this. Are we doing benefits of CTC minus benefits of colonoscopy?

DR. SINGH: Right. That's sufficient

evidence. Yes.

DR. MC NEIL: That's what we're doing? And

that's the --

UNKNOWN MALE VOICE: Is there evidence of?

DR. SINGH: Is there evidence of?

DR. MC NEIL: Evidence of both, that versus that.

DR. SINGH: Right.

DR. MC NEIL: That's what we're answering. Right?

DR. MOCK: And we've heard Dr. Singh say that there is documented evidence that optical colonoscopy has a net health benefit.

DR. SINGH: Correct.

DR. MORRIS: For polyps less than six millimeters.

DR. SINGH: No, no, no.

UNKNOWN MALE VOICE: Overall.

DR. SINGH: Overall, in the community.

DR. MORRIS: That's what the question is, though. Right?

DR. MC NEIL: The question is less than six.

We're answering less than six. Arden, you're right.

DR. MC DONOUGH: I believe there's evidence to inform the question. The only issue in terms of sufficient evidence is not the sensitivity and specificity for less than six millimeters. In fact, that might not be the most important question to inform sufficient evidence.

The sufficient evidence when you're detecting lesions which you're not going to remove is the harms of one test versus the harms of the other test in terms of the net health benefit because there are no positive net health benefits to detecting or not detecting six millimeter lesions. The harms are removing them and having an adverse effect.

UNKNOWN MALE VOICE: We don't have sufficient evidence to inform that.

DR. SINGH: We don't have --

DR. MC DONOUGH: Being exposed to radiation itself.

UNKNOWN MALE VOICE: There's not enough

evidence.

DR. MC DONOUGH: That's the explanation.

DR. MC NEIL: You know what? This is a little confusing. Let's move on and then come back to this and see where we want to end up. Yeah. Let's come back 'cause I think we're getting into a little bit of an issue with two and four.

But let's do six to ten, although that may not help us much.

UNKNOWN MALE VOICE: Six to ten?

DR. MC NEIL: We're doing six to less than ten. I'm sorry. Six to less than ten.

DR. MC NEIL: Maria, are you counting votes here?

DR. SINGH: Can I just say one issue only?

DR. MC NEIL: Say after we vote.

DR. SINGH: Okay.

(Whereupon, the panel voted.)

MS. ELLIS: We're fine.

DR. MC NEIL: Okay. Now, Dr. Singh?

DR. SINGH: You know, it was pointed out

that there is no evidence that polyps less than six millimeter have any -- have any relevance. This is a

paper that was published by Dr. David Lieberman (phonetic), and just recently published in CTH.

And he showed from the (unintelligible) that in the one to five millimeter group there was advanced histology in 1.7 percent of those polyps. So it's not a zero rate. It's a non-zero rate.

What I'm saying is that we can't just assume that anything less than six millimeters is benign and has no problems. We can't just assume that clearing the colon out of two or three or four millimeter polyps which endoscopists usually do has no benefit. So it's a non-zero rate.

DR. MC NEIL: (Unintelligible.)

DR. SINGH: It's a non-zero rate. Like I said, 1.7 percent. And considering the mortality from colonoscopy, we talked about 65 per 100,000 perforations. And out of that, I mean, I don't have the numbers here as to how many would actually die. But at good colorectal surgeons, not many would die.

So it's a very minuscule chance of that. So

versus 1.7 percent advanced histology in the small

polyps, and the unmeasurable chance of --

DR. MC NEIL: I think we saw -- I'm sorry to interrupt. I think we did see a -- I think in one of our pieces of information we saw something like that number. So we're not hearing it for the first -- I don't remember where it was. But it was in one of the pieces. So I think that should have been incorporated into our brain when we were voting.

Okay. Let's go to greater than or equal to six.

DR. SINGH: And I've just published in Gastroenterology last month, actually.

DR. MC NEIL: Well, I don't keep up with Gastroenterology, but I think in the book that we had --

So we're talking about greater than or equal to six. Greater than or equal to five.

UNKNOWN MALE VOICE: (Unintelligible.)

DR. MC NEIL: I'm sorry. Greater than or

equal to ten. Thank you, Steve.

(Whereupon, the panel voted.)

DR. MC NEIL: There are definitely some low markers and some high markers. But we'll see how they come out at the end. Okay.

So how about question three? That should involve a little less controversy, I think.

UNKNOWN MALE VOICE: Don't bet on it.

DR. MC NEIL: Don't bet on it. Okay.

DR. SINGH: Question three is controversial. It's exactly what I've been talking about, that how can we be sure that the evidence from colonoscopy will apply to screening CTC because colonoscopy not only detects but removes.

DR. MC NEIL: That's not what the question says.

UNKNOWN MALE VOICE: It's the modeling.

DR. MC NEIL: It's end modeling. So it would get at the kind of analysis that Dr. Zauber did.

Yes, Bob?

DR. MC DONOUGH: I have more confidence in

this because one of the things about CTC is it is

looking at sort of the anatomic lesion. It's not like

it's measuring something that's different than colonoscopy. I mean, there are some uncertainties about CT colonography, obviously. But it's trying to identify the same lesion.

It's not like comparing different biochemical tests that are different and, you know, may be related to heart disease risk that are, you know, diametrically different. It's the same kind of test.

DR. SINGH: True. But it doesn't remove those polyps. You're right. It detects the same.

DR. MORRIS: This question is not comparing to colonoscopy.

DR. MC NEIL: Read the question carefully.

DR. MOCK: It was my impression that we're not going to treat a 1.5 centimeter (unintelligible) polyp differently because it's seen on CTC than we are if we see it at endoscopy. The treatment of the polyp will be treated the same.

DR. SINGH: No. No. It's not. Because if a 3 millimeter polyp, if it is seen on a CTC, even if

it is seen, which it wouldn't be, but if it is seen on the CTC, that does remove. That does not go to colonoscopy. It's not removed. Whereas, at colonoscopy, it is removed.

UNKNOWN MALE VOICE: But this is --

DR. SINGH: It is (unintelligible). Modeling implies a benefit either. Actually, a modeling thing is where does the modeling data on colonoscopy come from? It comes from the net health benefits of colonoscopy. Colonoscopy is not just detection, but removal. So that's where it comes from.

See, that's the problem. We're sort of mixing the test with the procedure. Colonoscopy is both at the same time, and CTC is not.

DR. MC NEIL: Let me break that down, that question, into two parts. But we're not breaking it down, but just thinking about it.

If that question said, how confident are you

that the previous evidence and modeling for the

treatment of polyps greater than or equal to ten

millimeters discovered using other screening modalities, you would have a clear answer?

DR. SINGH: Yes. I would have a clear answer.

DR. MC NEIL: So now you're saying, but it's not just greater than ten millimeters.

DR. SINGH: Exactly.

DR. MC NEIL: And it might not even be just greater than six millimeters.

DR. SINGH: Exactly. And certainly not less than six.

DR. MC NEIL: So you want to fold into this question how confident are you that previous evidence and modeling for the treatment of polyps that don't even get referred to colonoscopy on the basis of colonography.

DR. SINGH: Precisely.

DR. MC NEIL: So that's --

DR. SINGH: You got it.

DR. MC NEIL: So this question is a mixture of two different components.

DR. SINGH: Right.

DR. MC NEIL: Is that right?

DR. SINGH: I agree. So if you divide it into three parts, A, B, C, then we can vote.

DR. MC NEIL: Steve has a question.

DR. PHURROUGH: I think the question -- and Barbara, this was your question, if I recall, so I can shift the blame here a little bit.

The question is, if you're developing a model for what's going to happen to a patient with a polyp, what's going to happen to a patient with a polyp, sort of the natural history of that patient is irrelevant to how that polyp is developed -- how that polyp is diagnosed, how do you find it.

Now, when we get into how you treat polyps that are diagnosed by different technologies, that, in fact, may change. But the natural history of that polyp, the question here, can you apply the same modeling that you applied to the diagnosis and

identification of that polyp using other technologies

to a polyp that's been identified using this

technology, do you need to change that modeling and --

DR. SINGH: So then I would change the question and say how confident are you that previous evidence and modeling for the treatment of polyps, instead of that, I would say for the natural history of polyps discovered using other screening modalities can be applied to people discovered using screening CTC.

Then that's the question that you're just asking. So instead of treatment, call it natural history. And I have enough evidence to vote on that.

DR. PHURROUGH: I guess I'm not -- I'm not --

DR. WEISSBERG: Could I just make the point that Dr. Rex, I think, presented the information about how many people would fall into that, you know, gray zone of having a couple of intermediate size polyps, but perhaps with advanced histology. Isn't that the data that he presented earlier?

DR. SINGH: I don't think he presented Dr. Lieberman's data.

DR. CASH: I presented Lieberman's data from the Gastro article from last month which they looked at the (unintelligible) database.

DR. SINGH: Right.

DR. CASH: And they found a zero percent risk. They did find one cancer in diminutive polyps. By diminutive, I mean five millimeters or less. But the percentage rate was zero.

DR. SINGH: 1.7 percent.

UNKNOWN MALE VOICE: But your point is --

DR. SINGH: The advanced histology.

DR. CASH: You're talking about a different study. We're talking about two different studies by Lieberman, I believe.

DR. SINGH: Okay. I'm talking about this one.

DR. WEISSBERG: But this basically comes back to the issue of whether a patient will be sent on to optical colonoscopy and then would perhaps benefit

from removal of all lesions identified as opposed to

whether they just had, you know, a few little

diminutive polyps that weren't called on virtual colonoscopy that then impacted their life. That's what you're talking about.

DR. PHURROUGH: But again, what we're attempting to do in this broad discussion around whether we should pay for this or not is to take into account not just -- we look at what would happen to a patient who has a polyp identified regardless of how that polyp is identified.

And the modeling doesn't change if you determine that, in fact, for this group of patients I'm not going to do anything for the three millimeter polyp because we know in general -- if we know in general what happens to a three millimeter polyp that's identified by CTC -- by optical colonoscopy, the same thing is going to happen to that polyp that's identified by CTC, the modeling can take account of we're not going to refer those forward if they're less than five.

The modeling doesn't change. You just --

you just say, in this group of patients we're not

going to send them forward. So treatment is considered in the models. I can't say that the models are -- the modeling itself would change. Just the inputs into the model would change.

DR. MC NEIL: I think we can say it might be slightly different. He might be saying that -- what you said is correct. But he might say that if a colonoscopist is in there, I think you're saying, and sees a three millimeter or four millimeter or five millimeter polyp, he might snag it.

DR. SINGH: Exactly.

DR. MC NEIL: Whereas that patient would never have gotten referred.

DR. PHURROUGH: The model can address that. There's nothing about the model that would --

DR. PEDEN: I think the only data that we heard today and the only data that's in our packet that makes me question whether there's sufficient evidence here as far as, you know, Dr. Phurrough, what

you said about the management from a natural history

perspective, is the point that I think Dr. Rex made

which was what do you do with the patient who has a positive finding on CTC, goes to colonoscopy, and they don't find anything.

I think that's the only place where we don't necessarily have sufficient evidence, that scenario where there's no current modeling or predictive studies that lets us make a decision about the way to manage that patient.

DR. MC NEIL: Did you want to say something?

DR. ZAUBER: I wanted to say something, but not specifically about that.

What we modeled was a strategy. And the strategy was for CTC was if it was a six millimeter lesion or greater, it was referred on to colonoscopy. And that was optical colonoscopy. And indeed, all polyps detected were removed.

That included picking up some hyperplastics. It certainly included picking up some small adenomas that were -- that was not seen on CTC. So it is a

20 combination that's the strategy of starting with CTC

21 and then going to optical colonoscopy. It's the same

strategy if you're doing FOBT. You have a positive FOBT, it goes to full colonoscopy.

So there are some of the small adenomas that are detected from CTC referral. I don't see --

DR. MC NEIL: But those haven't been modeled. Is that correct?

DR. ZAUBER: No. They are modeled. Because the natural history is there. Those adenomas are going through. And you've got a probability of having it referred. You've got a specificity issue on CTC, so you're going to have some false positives.

So the model takes through whatever adenomas are there, and they keep growing to a certain degree. Certain ones will end up going into colon cancer. And then you overlay back the intervention of the CTC finding them and the intervention of colonoscopy taking them out.

There's also the interval -- the big question is the repeat interval because we say --

DR. MC NEIL: But that's not --

DR. ZAUBER: -- small adenomas don't matter.

Well, if you go forty years, they matter. So you know, you go ten years, they matter. So you have to take into account the strategy that includes some repeat.

DR. MC NEIL: Okay. That's very helpful. Thank you.

DR. PHURROUGH: I think you just made a very important point, that we have yet to discover -- to determine how do you model that group of patients who are positive CTC and negative OC.

DR. MC NEIL: Well, I think what Ann just said is they sit tight. They don't get referred on, and their adenoma grows for five years, I think is what you implied.

And there's a certain probability that after five years, that four millimeter adenoma is going to become ten millimeters, and boom, there's an X percent chance that's going to be cancer. And you model that all in.

DR. PHURROUGH: We don't even know if it's an adenoma yet or not.

DR. MC NEIL: No. No. We don't.

DR. PHURROUGH: You just know it's an abnormal CTC.

DR. MC NEIL: We just know it's an abnormal CTC.

DR. MOCK: I'd say what Jerry is talking about is we don't know how to model false positives.

DR. PEDEN: Correct. That's correct.

DR. MC NEIL: No. No. That's not true. You do know. That's not true. She does.

DR. ZAUBER: If you saw it on CTC, you go back for it, maybe you didn't see it on CTC. The natural history is still going there. And there are going to be some times that you miss something.

Both -- optical colonoscopy is going to miss it. I mean, you know, when you get to the smaller adenomas, we're only going at 75 percent detection, 85 percent detection for the medium size. So there can be a missed adenoma. There can be a missed cancer

with optical colonoscopy as well.

You've got the natural history moving

forward. CTC interrupts it by sending lesions greater than six millimeters -- six millimeters or greater on to optical colonoscopy. At which point, whatever optical colonoscopy can see and remove are removed.

DR. SINGH: If we change this question and call it natural history --

DR. MC NEIL: No.

DR. SINGH: Because then the answer is clear.

DR. MC NEIL: No. I think it's clear the way it is, actually. I think she was very clear on what the model is doing. At least, I think. Maybe I'm wrong.

UNKNOWN MALE VOICE: Let's vote.

DR. MC NEIL: You want to vote?

UNKNOWN MALE VOICE: Let's vote.

DR. MC NEIL: Let's vote. Okay.

(Whereupon, the panel voted.)

DR. MC NEIL: Okay. Are we ready to move

on? So this next question has some -- the fourth question has some discussion questions which are in

our book. But we actually discussed them all, I think.

But let's look at the question and then see if we need to go back to the discussion questions. Does that make sense? So now we're going to look for net health benefits going back for the point that was a little confusing earlier. We're not looking -- so the evidence, whether the evidence is there to determine. We're looking, is there a net health benefit?

So how do we feel?

DR. MORRIS: When you say health benefit, you mean net health benefit?

DR. MC NEIL: It's net. It says net. Net is written here.

DR. MC DONOUGH: So your confidence about a net health benefit can be affected both by the strength of the evidence, but also about your weighing of what has been proven about the benefits versus the

20 risks.

21 DR. MC NEIL: Well, we did the strength in

the earlier question.

DR. MC DONOUGH: Okay.

DR. MC NEIL: That was question two. Right?

DR. WEISSBERG: We didn't vote on the strength of evidence on the harms.

DR. MC NEIL: I'm sorry, Jed?

DR. WEISSBERG: We didn't vote --

DR. SINGH: That's not a question.

DR. MC NEIL: You're right. It's not a question. I'm sorry. You're right.

DR. SINGH: But that's an important question. Isn't it? About the evidence on the presence of harms. Shall we add that question?

DR. MC NEIL: No. Net always implies harm. Net implies harm.

UNKNOWN MALE VOICE: Net implies harm.

UNKNOWN MALE VOICE: How confident are you that there's a net health benefit?

DR. MC DONOUGH: But I guess what I'm saying

is that your answer to question four is affected --

the confidence that you have that screening CTC has a

similar net health benefit to optical colonoscopy is affected both by your confidence in the evidence --

DR. MC NEIL: And isn't that in question two?

DR. MC DONOUGH: -- as well as your weighing of the benefits versus the harms.

DR. MC NEIL: Correct. That's correct.

DR. PHURROUGH: Is there evidence, and am I confident in what that evidence demonstrates?

DR. MC NEIL: I mean, I assume if you answered a one in question two, it would be mighty hard to get up to a five in question four. Right? No?

UNKNOWN MALE VOICE: Question two has certain (unintelligible).

DR. MC NEIL: Oh, that's true. That's true. Okay. So net health benefits relative to optical colonoscopy, considering benefits and harms. And the harms we've enumerated already. But we could go

through them again. But we, I think, talked about the harms enough.

DR. PEARSON: And for the sake of argument, it also includes our judgements about the generalizability of the results to the practice. I mean, in terms of interpreter training, technical aspects of CTC, and the follow-up of patients with polyps, I think it's all wrapped into this net health benefit judgement.

DR. MC NEIL: That's correct.

DR. SAMSON: I'd like to make a comment. The way I'm interpreting this question is that it's sort of one step before question five that takes into account cost.

And so for me, the net health benefit is the cost-effectiveness model minus the costs and looking at life-years gained. The net health benefit takes into account a lot of factors. You know, the sensitivity, specificity, all of the outcomes associated with screening, the outcomes associated with treated colorectal cancer.

But the only things that aren't taken into account in the model were the impact of extra-colonic

findings and radiation risks. And to me, this question asks can we go forward with a judgement about this without having more information about those two question marks. And is it possible that those two factors, you know, might be negligible enough that we can have confidence in the cost-effectiveness model.

DR. SINGH: I see this slightly differently. You know, what you're saying is that obviously based on the following question, how confident are you that the evidence demonstrates CTC results in a modeled net health benefit, we're not talking about a modeled net health benefit 'cause what we're synched to is a modeled net health benefit.

We're talking about a demonstrated net health benefit. Are we there yet? Again, maybe I come from a different world. You know, a come from a regulatory world where it's like a show-me thing. Show me.

DR. SAMSON: Right. I would counter that,

you know, the USPSTF approach is that sometimes direct

evidence is required, and sometimes you can piece

together within an analytic framework. And the cost-effectiveness model was an analytic framework approach. And that, you know, to expect a randomized trial on CTC is probably unrealistic.

DR. MC NEIL: Steve?

DR. TEUTSCH: As I look at this, I say, well, you know, what we've seen is, in general, it appears the benefits are really pretty similar when it comes to the colonic findings. The extra-colonic benefits or harms, we really don't know.

And if you think -- it's a confidence interval question. And you could sort of say, gee, one is big confidence interval and one is small in terms of what you think the harms and benefits are. But they still may be similar.

But if you think that there -- at least in my mind, some of these things are more important. And if you think there are potential harms that are potentially large, and the benefits are the same, then

I would say that we have a fairly level of certainty as to whether they are similar.

That's how I look at it. Because I don't have confidence from what I know that the harms which are really of more concern to me than the extra-colonic benefits. I guess people have to decide whether, based on what they've seen, that they see those harms as potentially big or not.

DR. MC NEIL: And the harms you're particularly concerned about?

DR. TEUTSCH: I'm particularly concerned about the extra-colonic findings. And I'm worried about people finding Triple-A's and going in and, you know, however the test is and doing them. We don't recommend screening for Triple-A's except in 55 to 65 year old smokers -- 65 to 75 year old male smokers.

So if that's where you start, you sort of say, well, you find these things, you're going to do things. The harms are potentially large, even for you, going in and finding other lesions.

So that's how I look at it. I think the

question really is the benefits of these things on the colonic side are fairly -- probably close. And it

really is how do you perceive the harms. I don't particularly think that the cancer risks are big with the radiation. But the other potentially is. Others can obviously look at it differently.

DR. MC NEIL: Mike?

MR. LACEY: I would ask a question related to the Triple-A. Didn't Medicare just institute a Triple-A screening benefit for entry into the program? So in a sense, you're going to be trying to find Triple-A, and you're going to have watchful waiting or intervention based on whatever the morphology of the patient is.

And to find a few of them on CT doesn't seem to have any harm possibility because you're going to be -- you're basically just making a more efficient finding rather than having to do the entry triple-A exam. Right? I mean, isn't that accurate?

DR. MC NEIL: Yes.

DR. PHURROUGH: Assuming there would be a

hundred percent uptake of that Triple-A screening, and we're somewhere in the ballpark of next to none.

MR. LACEY: But the point is, it's a policy point to do it. So I don't understand --

DR. TEUTSCH: It allows them to do it. The question is, you know, should they do Triple-A screening, and then the answer, at least, in the Preventive Service Task Force, it's a fairly limited group that should be screened.

And here's now you're going to potentially with perhaps a suboptimal test screen a whole lot more people that you otherwise wouldn't have looked at for Triple-A. You're going to find these things whether you wanted to or not if you do CTC.

MR. LACEY: But what's the most common thing to do after you find Triple-A? It's not to intervene. It's watchful waiting. It's to follow it.

DR. TEUTSCH: It depends how big they are. Doesn't it? It depends how big they are. And if they're small, yes. And if they're big, you presumably do something about it.

MR. LACEY: But shouldn't that be happening?

If people are walking around with big aneurysms,

aren't they at extreme risk of immediate death anyway? So why wouldn't you want to intervene? I'm not sure I'm understanding the risk here.

DR. TEUTSCH: Because when the studies were done, they showed that really the only benefit of screening was in those smokers. And I can't remember if that was because of the rate of large aneurysms. Is that what it was? Or it was the risk of them rupturing, I think. It was as much the risk of them rupturing which was greater in male smokers than it was in females, who, if I remember right, had a net harm.

DR. SINGH: This is why you need evidence, not analytic evidence and not modeled evidence, you know.

DR. MC NEIL: All right. We've got that point.

DR. SINGH: Even if we --

DR. MC NEIL: We got it. Hold on. Let's

move on. We've got a bunch of other people who want to talk. Steve and then Cliff.

DR. PEARSON: I'm glad Steve framed it this way. I mean, at the end of the day, it often happens evidence based medicine ends up with the pixie dust of just gut values about how you weigh some of the areas.

And I have to be honest. I just doubt we will ever have what many people would consider adequate evidence. And incidental findings and radiation harm are the burden that most diagnostic radiologic studies have to bear.

So for me, one of the key words in this question is similar. And it has to do with the boundaries in which -- Steve Teutsch sees the potential for, you know, relatively significant harms. I personally tend to see that there will be some harms, but there will be some benefits.

I actually would personally probably guess that it'll be a net harm just on the incidental finding side. But I'm actually personally not convinced that that net negative will throw it out of

the similar camp when you're looking at the bigger picture.

So I guess one of the questions -- again, we could argue all day because there really isn't adequate evidence about whether it's a net benefit, an equal benefit, or net harm. But the real question is, do we think that our confidence interval, our conceptual confidence interval is that it will be so negative as to no longer create a similar overall judgement. At least, that's the way I'm looking at it.

DR. MC NEIL: Cliff?

DR. GOODMAN: We couldn't have planned this better insofar as the sequence of questions.

DR. MC NEIL: Thank you. We really worked hard on that.

DR. GOODMAN: I need some clarification on similar. Net health benefit for Medicare beneficiaries is similar, not relative, to optical colonoscopy. Are we comparing -- when we talk about net health benefit, are we talking about CTC versus no

screening, FOBT, flexible sigmoidoscopy?

DR. MC NEIL: No. No.

DR. GOODMAN: We're talking about it relative to optical. Okay. Fine. Good. That's harder to prove than relative to those other things.

DR. MC NEIL: No. Understood.

DR. GOODMAN: Thank you. I needed that.

Then the second one is, on the 95 percent confidence interval thing, if I were modeling this, and I put 95 percent confidence and rules around all these variables, and then tried to disprove the Null hypothesis that CTC was the same as optical, I'd never get out of the confidence interval.

That confidence interval would be very, very wide. It would be very hard to push off the Null hypothesis that they're the same. Okay? So the pixie dust is going to have to apply here. I haven't modeled it. I suspect if I did, we would have a very hard time with the available evidence to prove a true difference between the two. Think of all the variables we've put on the table here.

DR. SINGH: May I say something?

DR. PHURROUGH: Not to add complexity to

this. But why not? We're paying you well.

DR. MORRIS: Lunch was great.

DR. PHURROUGH: And you paid for that. We do reimburse you for lunch. Don't we?

There are four discussion questions here. And we've actually spent most of the day on those four discussion questions. But they're here for the purpose of causing you to think about does your decision around how confident are you in a net health benefit requires the CTC and its strategy of follow-up to meet certain parameters.

So do you have to have a trained radiologist to draw your conclusions of a confidence in net health benefit? Do you have to have a certain level of a machine to get your same level of confidence?

So those questions are added in here so that you can advise us a bit more as to if, in fact, we should decide that this is a benefit we want to offer to the population. Do we need to put those parameters

20 around it, that it needs to have a certified provider,

21 it needs to be on at least a 16 slice scanner or a 64

slice or whatever you say.

So those parameters are to be part of your thinking about how you want to vote on this.

DR. MC DONOUGH: Well, just as an example, another example, you know, whether you're going to have available optical colonoscopy on the same day.

DR. MC NEIL: All of that is in here.

DR. PHURROUGH: Exactly.

DR. MC NEIL: The other thing that has an impact on this that we haven't mentioned so far is -- it comes in later in question number seven, but it does get imbedded in question number four -- is are you going to be screening more. So that you are going to pick up a few more cancers that might tip the balance a little bit relative to the harms that Steve is particularly worried about.

All right. What more do we want to discuss? I'm looking at my clock, and I know in twenty minutes two people are going to leave, if not three.

UNKNOWN MALE VOICE: So let's vote.

DR. MC NEIL: So this is the tough one. I

agree with that. The others are pretty easy. Is there anything more to say about this one, or are we --

DR. SINGH: Do we want to work through discussion questions, too?

DR. MC NEIL: We did those already. Didn't we? I thought we obsessed about them, actually.

DR. SINGH: Okay.

DR. MC NEIL: I don't want to obsess any more. But if you want to, we can still go back to some of them, if you'd like?

Are we ready to vote?

UNKNOWN MALE VOICE: Uh-huh.

DR. MC NEIL: Okay.

(Whereupon, the panel voted.)

DR. MC NEIL: Got it? Okay. Number five. That's easy. Right? We don't even have to discuss that. Or do we?

DR. WEISSBERG: I think we have to discuss

that.

DR. MC NEIL: Pardon? I mean, wasn't there

a little point on a graph that gave us the answer?

DR. WEISSBERG: Well, we were presented evidence that it doesn't have the same cost.

DR. MC NEIL: Right. Exactly.

DR. SINGH: Exactly. So it's one.

DR. MC NEIL: So it's one.

DR. WEISSBERG: We have no confidence that it's true.

DR. SINGH: The answer is one.

DR. MC NEIL: Isn't this absolutely one?

DR. MORRIS: No. It depends on adherence. So it was modeled on a 50 percent adherence rate. But if adherence is really 60 percent which, you know, a lot of data shows that adherence is 60 percent. At 62.5 percent, it was -- wasn't it superior at 62.5 percent?

DR. MC NEIL: No. It was still -- it was still --

DR. SINGH: Better at 25 percent. Yes.

DR. MC DONOUGH: If you increased the adherence by --

DR. SINGH: 25 percent improvement in compliance. That means you would increase the screening in the population by 25 percent.

DR. MORRIS: Yes. I understand that.

DR. SINGH: That's huge. Wow.

DR. MORRIS: I thought it was modeled on 62.5 percent.

DR. ZAUBER: There's a 10 percent increase over the baseline at 50. Baseline model (unintelligible). The baseline model says everything is at 100 percent. The sensitivity analysis that has to do with adherence adjusts everything to be equal at 50 percent so that you can then ratchet them up and down.

DR. MORRIS: Right.

DR. ZAUBER: And then leave colonoscopy and all of our other methods at 50 percent, you give a 10 percent advantage (unintelligible) 55 for the --

DR. MORRIS: You're making the assumption

that with CTC that adherence goes up by ten percent.

UNKNOWN MALE VOICE: Ten percent more people

will avail themselves --

DR. MORRIS: And that gets you partway to over the line. And then when it goes up by --

DR. SINGH: Twenty-five percent.

DR. ZAUBER: (Unintelligible.)

DR. MORRIS: Okay. No. I understand. I understand that when you get better adherence --

DR. SINGH: What happens on the other two models?

DR. BARTON: One at a time. Hold on. One at a time.

DR. SINGH: That's an important consideration. So on the other two models, it's not the same.

DR. ZAUBER: They're all in the same ballpark.

UNKNOWN MALE VOICE: Not quite as high.

DR. MORRIS: That's just a variable --

DR. SINGH: My point exactly. So that's the

most optimistic scenario.

DR. ZAUBER: I would have to check.

DR. MC NEIL: Let her check, and let's ask for other questions. Yes, Mike?

MR. LACEY: Well, in the people in the increased compliance group, then is the comparator that there would be new patients so the comparator is against not screened? In which case the cost-effectiveness ratio would be more similar to optical colonoscopy which we talked about a little earlier, which is, you know, $30,000 per life-year saved as opposed to say $22-.

If you're talking about it marginal to optical colonoscopy, then it's whatever, $300- per life-year saved, which was what was presented.

But if you're talking about giving it a -- pulling in an extra five to ten million people or whatever, your proper comparator is against no screening at all, in which case, this would clearly be a cost-effective approach.

DR. MC NEIL: That's what she was talking

about.

DR. SINGH: That's what she was talking

about.

MR. LACEY: So it's not a straightforward answer, I guess.

DR. MC NEIL: Well, I thought -- I thought if you looked at her slides --

MR. LACEY: To answer this question, I guess the question -- are we saying that if it's just for the same patients who -- you know, it's comparison of you're replacing a colonoscopy with a CTC. That's not cost-effective. Or if you're having it as a complement, it is cost-effective.

DR. MC NEIL: I thought she -- if you took a hundred patients in the normal situation, 50 of them got screened with something or other. And then if you were able to increase it to 55 percent by CTC, you got the results. And if you were to increase from 50 to 62 percent, you got above.

DR. ZAUBER: You got above. And that is true of all the models. If you can get a 25 percent

differential adherence for CTC over another test.

DR. SINGH: Right. So basically it means

that if you offer a test to 100 people and only 50 people accept colonoscopy, but 62 and a half accept CTC.

MR. LACEY: And I'm asking what's the proper comparator. The issue is that the efficiency curve is an average number. Right? And when you're talking -- you haven't done the ratio. You haven't done the efficiency ratio of cost to life-years gained. Right? And so that's -- you laid it out in the curve.

My point is, if your comparison is against optical colonoscopy, you would be looking at roughly the same effectiveness to a big delta in cost. Right? But if you're comparing it against no screening, it's a big difference in both.

DR. MC NEIL: This is against optical colonoscopy.

MR. LACEY: What I mean is, it's implied if you have an increased compliance, and you're bringing in more patients, the proper comparitor would be

against no intervention at all, in which case it is highly cost-effective.

DR. SINGH: Let me try to explain this. So what she is doing is she is --

MR. LACEY: I understand it.

DR. SINGH: -- comparing against no intervention. So she is comparing colonoscopy versus no intervention, CTC versus no intervention. And then she is assuming that CTC brings in 25 percent more people. So at a population level, that 25 percent more versus no screening.

MR. LACEY: That's what I just said.

DR. SINGH: Exactly.

MR. LACEY: But my point is that it's a highly cost-effective intervention with the assumption that you're bringing in more patients.

DR. SINGH: Exactly. If you do.

MR. LACEY: So how do we answer this question?

DR. SINGH: If you assume --

MR. LACEY: The question is not clear

because it has to be broken into two points because

you have two comparators.

DR. SINGH: But that's the next question. That's the next question. Do you actually bring in more people?

DR. ZAUBER: That's important because we're looking for ways to reach the efficiency level.

MR. LACEY: At the same level, it's clearly more expensive. Well, I guess my point is you solve for price as opposed to solving for effectiveness.

DR. SINGH: Absolutely. There is no evidence --

DR. MC NEIL: Shhh. There are too many conversations going on at one time. Could we start -- Mike, start and finish.

MR. LACEY: I'm done.

DR. MC NEIL: You're done. Steve, you're next. Start and finish.

DR. PEARSON: Okay. I am going to pick up. I think the way this is worded is what you were saying. It's comparing it to no screening.

Obviously, colonoscopy, you know, saves life-years at a certain cost. CTC also compared to no screening

saves lives at a certain cost. And I think that the question again is how do we get it to, quote, unquote, "the efficiency frontier" if we want to compare the two.

I mean, they are similar relatively when you compare them to no screening. They're both extremely effective and at a relatively low cost per life-year saved. So -- but I'm actually not so, in this case and for this question, interested in the hypotheticals about whether they're going to bring in more people or not.

I just want to make the point that I still think that this is a little bit misleading to talk about current Medicare prices given that we've just identified that anesthesia costs are an important variable that have not been left in.

I wish we had worded this in a ratio perspective because, again, whatever the cost of optical colonoscopy is where you are practicing with

your Medicare patients, you want to compare the cost

of CTC to that to judge whether it is relatively cost-

effective or not, comparatively.

So as it's worded, I would say that compared to no screening, they both do have relatively similar ratios of cost per life-years saved. Again, that's to no screening.

And if we're going to talk about --

DR. MC NEIL: How did you get that, Steve?

DR. PEARSON: Well, because they both save actually almost the same number of lives.

DR. MC NEIL: Are you looking at this graph here?

DR. PEARSON: Yeah. I mean, the difference is between, what, $1,000 to $2,000 per life-year saved?

DR. SINGH: That's double.

DR. MORRIS: (Unintelligible) dollars per life-year saved?

DR. PEARSON: That's not -- in the big picture, that's not a big --

DR. SINGH: It's a hundred percent difference.

DR. MORRIS: Did you just figure out what the cost per life-year saved is in your study for colonoscopy?

DR. MC NEIL: $2100.

DR. ZAUBER: (Unintelligible.)

DR. MORRIS: I just can't divide right now.

DR. ZAUBER: What we were asked to do was to really look at it in terms of incremental (unintelligible) ratio (unintelligible) efficiency frontier. And then in the secondary analysis we were asked to compare the optical colonoscopy (unintelligible).

So that's the -- we're looking at the efficiency frontier (unintelligible) what are all the options out of there and what is (unintelligible). And that was one answer. (Unintelligible.)

DR. PEARSON: But to the -- and you can correct me if I'm wrong about anesthesia.

DR. ZAUBER: (Unintelligible.) The prices

here include the physician and this will include

pathology fee. It does not include an additional fee

for anesthesia. It does include the (unintelligible). It's also from the Medicare perspective, what they'll pay for.

DR. PEARSON: I think, again, maybe I'm beating a dead horse, but the perspective is just incredibly important here. If you look at either of these interventions against no screening, and even over the age of 65, you're gaining life-years at what is considered by health economists to be a very low price.

In 50 years old and above, we actually found that it was cost saving. Either one. These days, with the cost of treating colorectal cancer, either one is actually cost-saving.

So if you compare them -- again, they're cost per life-year saved of CTC and of colonoscopy to nothing, it's going to be in a narrow range of $1- to $2,000, $2500 per live-year saved.

Again, if you want to now talk about

incremental cost-effectiveness relate to each other,

that's different. It's going to be a much higher

number because, again, their effectiveness is very similar.

But the only issue I wanted to raise was that I think it's dicey for us to say anything about that too definitively given the uncertainty around the anesthesia component of the cost. We might want to talk about ratios. But that was the main point I wanted to make.

DR. MC NEIL: Other comments here?

DR. ZAUBER: (Unintelligible.)

DR. MC NEIL: Sure.

DR. ZAUBER: It's not exactly the same. If you want to go back to the number of life-years saved (unintelligible), you can see it on the chart, they're not the same. The life-years gained are comparable (unintelligible). But with the price of $488, they were definitely much more expensive (unintelligible).

MR. LACEY: I guess they define a lot more. I mean, the question is, you know, if you do the

ratio, both strategies are well below the accepted threshold of $50,000 dollars per life-year gained.

And I think that's all his point was.

DR. MC NEIL: But I think that's not what the question is.

DR. SINGH: But that's not what the question is.

DR. MC NEIL: That's not what the question is. I think you're right. By any metric, this is a terrific value. Either test has terrific value associated with it and could be cost-saving given the price of drugs for colon cancer, at least advanced stage colon cancer.

So take that one off the table. Agreed. We all agree this is cost -- you know, if we're looking at relative to other things that we spend money on, this is cheap. That's not what the question is.

The question is, you know, read it. How confident are we that CTC is a similar ratio of cost per life-year saved. It's not cost per quality adjusted that we're looking at here. We're just

looking at is -- do you get the same -- basically, I think the question is asking about the sensitivity

analyses that were done, going from 50 percent to 55 percent to 62.5 percent, something like that.

Now, the anesthesia costs are a different wrinkle. And it's obviously going to be a little bit -- it's not going to be quite a two to one ratio or whatever it is. That would require a little bit more modeling to get there.

But maybe for the sake of discussion here, we should answer this question as it is written without anesthesia costs 'cause we don't have those data, and have a little footnote to Steve and his group that these data we believe may be limited because they don't fully incorporate all the costs of optical colonoscopy.

I don't want to fudge and make up numbers and make up ratios when we don't have them. Let's answer the question. Put a note, say we don't love all the data that we have because we -- new thoughts have come to mind. And let's just answer this one as

it is, given the analysis that we have.

So the question therefore on the table is

how confident are you that a similar cost per life-year depends not only on the graph, but withdrawals or not we think there will be different take-up rate. And if there's a different take-up rate, whether -- is more than 10 percent -- 10 percent or more than 25 percent over the base case.

I mean, that -- or if it's zero percent over the base case.

DR. ZAUBER: I would just say that's a hypothetical (unintelligible). You don't have evidence --

DR. MC NEIL: I know. Of course you don't. We're well aware of that 'cause we beat that horse this morning.

DR. SINGH: Did you model colonoscopies every five years as well, or you didn't do that?

DR. MC NEIL: She can do anything.

DR. ZAUBER: Did we model colonoscopy every five years?

DR. SINGH: Yes.

DR. ZAUBER: (Unintelligible.)

DR. SINGH: And when you model it every five years, then what happens to this ratio?

DR. ZAUBER: We didn't do cost.

DR. SINGH: Oh, you didn't do the cost. Okay.

DR. ZAUBER: (Unintelligible.)

DR. WEISSBERG: I'm sorry. I'm still a little unclear.

DR. MC NEIL: Yes, Jed?

DR. WEISSBERG: The point you were raising was question six, isn't it, whether you bring more people into the screening population?

DR. MC NEIL: Well, I was. But in some sense when you talk about current Medicare prices, it turns out that the -- moving to be the efficient frontier, the price at which you move to the efficient frontier varied with the number of people you brought in.

MR. WALTER: But I would word question five

-- I would add the wording, all other things being

equal, meaning the same.

DR. MC NEIL: All right. Okay. Fine.

DR. SINGH: Okay.

DR. MC NEIL: Okay. That's fair, Jed.

DR. WEISSBERG: But then the question is, I mean, we're not making our own sort of estimates here about harm from radiation or extra-colonic findings. These are dollars. So then we have to say, what dollar range do we call similar.

And we were hearing that a couple of thousand here or there is similar to some people, but not to others. So I'm confused.

DR. MC NEIL: I think what the issue --

DR. WEISSBERG: So --

DR. MC NEIL: Hold on. Hold on, Jed. I think the cost there was, is the price of CTC in the current model lead to a similar value. And she was basically saying you go from $488 -- to get on the efficient frontier, you need to drop the price of CTC from $488 to $200 or something like that, all other

things being equal.

DR. SINGH: So we already have that answer.

DR. MC NEIL: Is that right? Do I have that right?

UNKNOWN MALE VOICE: (Unintelligible.)

DR. MC NEIL: So just to be clear on where we are on this question, for question number five, it's all other things being equal, as you said, and with the note that the cost analysis that led to the efficient frontier and to the sensitivity analysis may not have included some of the other costs that Medicare would pay even though they're not quite under the colonoscopy rubric. That is, for certain parts of the country, there's an anesthesia component as well.

But that's not for this. We're just going to look at the data that we have here. Is that a --

DR. MORRIS: Can you answer a clarifying question? So for five, then we're just assuming that -- in answering this question, we're assuming that CTC does not improve adherence.

DR. MC NEIL: That, I think, is what we just

decided. I think that's what we just decided. It's cleanest if we do that, Arden.

DR. MORRIS: Okay.

DR. MC NEIL: And I muddled it, and I apologize. So we'll just not look at your sensitivity analysis at this point. We'll just look at whatever figure number this is.

UNKNOWN MALE VOICE: The base case.

DR. MC NEIL: Are we all set? So the question is, how confident are we? All right. Let's vote.

(Whereupon, the panel voted.)

DR. MC NEIL: Okay. Question six, will it increase screening rates?

DR. SINGH: No data. No data.

DR. MC NEIL: Does that take care of that one?

UNKNOWN MALE VOICE: (Unintelligible.)

DR. MC NEIL: We're going to vote.

UNKNOWN MALE VOICE: Vote.

DR. MC NEIL: All right. Vote. How

confident are we?

(Whereupon, the panel voted.)

DR. MC NEIL: Okay. Number seven, how confident are you that there is sufficient evidence to determine the appropriate CTC guidelines for referral for polyp removal and frequency of screening?

MR. LACEY: Can we split those?

DR. SINGH: No. You cannot split those.

DR. MC NEIL: Can we split them, Steve? Sure. So 7-A is polyp removal and 7-B is screening. I'm sorry. Frequency of screening. Right?

DR. MORRIS: Say that again.

DR. MC NEIL: 7-A is now appropriate CT guidelines for referral for polyp removal. And 7-B is CT guidelines for referral -- for frequency of screening. Okay? Who would like to discuss polyp removal?

DR. SINGH: Well, I guess polyp removal is any polyps six millimeters or more will be removed. So anything you see, you will remove. You'll only see more than six millimeters, so you remove it.

DR. MC NEIL: So you like the guideline?

DR. SINGH: So it's very simple. Right?

DR. WEISSBERG: I would suggest that the referral is to a gastroenterologist to discuss colonoscopy to remove a lesion. And there's always the option of deciding to do it, wait, re-test later.

DR. MC NEIL: Well, I assume for referral means that.

DR. SINGH: Yes.

DR. WEISSBERG: But it's not necessarily going to eventuate in polyp removal.

DR. MC NEIL: Okay. True. True. So referral to a gastroenterologist for discussion about polyp removal.

DR. PHURROUGH: Well, it doesn't necessarily say that anyway. The question is, do we know whether someone with a polyp less than six ought to be referred or not.

UNKNOWN MALE VOICE: We don't know about patients --

DR. SINGH: We don't know that.

UNKNOWN MALE VOICE: We don't have any data.

DR. PHURROUGH: Well --

UNKNOWN MALE VOICE: It won't be reported.

DR. SINGH: Okay. Now, that changes a lot.

DR. PHURROUGH: I'm the primary care doc. I've got a CTC in front of me that says we found a polyp four millimeters in size.

UNKNOWN MALE VOICE: It won't say that.

DR. PHURROUGH: Do we know enough to create a guideline that says do or don't send that patient to a gastroenterologist for evaluation?

DR. SINGH: That's a very different question. That is probably a far more important question than the way I understood it.

DR. PHURROUGH: So what does a primary care doc do with a CTC scan that says four millimeters? Do we know enough to create a guideline to tell him what to do?

DR. WEISSBERG: I was operating under the assumption that we're listening to the ACR and AGA recommendations about reporting, which would not

20 report that. Wouldn't it?

21 UNKNOWN FEMALE VOICE: It wouldn't report

it.

DR. WEISSBERG: Right. So we wouldn't be faced with that situation.

DR. SINGH: No. But shouldn't we report it? That's what (unintelligible) said, that you should report everything. You should tell a patient everything. And I bet you (unintelligible), probably everybody will. You know, what is that little four millimeter thing --

DR. KLEIN: In all fairness, the problem is you don't -- the reason you don't report isn't because you want to keep it a secret from the patient. It's because you can't reliably differentiate a small amount of residual fecal material from a polyp.

So that's why you don't report it. And you worry about harm. And on the one hand, you worry about harm, well, this could do harm. Right? So that's why we like to try to minimize any potential harm.

And so the chance of having a significant lesion is a four millimeter polyp is so remote, then

that's why we've decided collectively among radiologists to not report polyps less than five millimeters.

DR. PEDEN: So do you really not report it, or do you have a sentence that you routinely report that questions the lack of reporting, if I'm making any sense?

DR. KLEIN: I have a comment in my report that says, polyps less than five millimeters are not reported since they cannot be reliably differentiated from retained fecal material.

DR. SINGH: So Steve, how would you change the question now? Would you say only --

DR. PHURROUGH: I wouldn't change the question. I think it was a great question.

DR. SINGH: How would you change the (unintelligible). You gave us a scenario that if a family care physician looks at a report of a four millimeter polyp and doesn't know what to do with it.

DR. MC NEIL: He's not to get it.

DR. SINGH: He's not going to get it. So

how would you change that framing? I want Steve to reframe that question because that totally changed my answer.

DR. MC NEIL: No. Can I just interrupt? I thought what we just heard is the referring doc is not going to get -- in general, he or she is not going to get a report that says there was a four or a five millimeter polyp.

DR. PHURROUGH: From Dr. Klein.

DR. MC NEIL: But that's the guideline?

DR. KLEIN: That's also the essential standard that we've met -- you know, that organizations are promoting. So it's not just my opinion.

DR. MC NEIL: Does everybody else --

UNKNOWN MALE VOICE: (Unintelligible.)

UNKNOWN MALE VOICE: I think you got (unintelligible) so upset that they left.

DR. KLEIN: I can give you my word that

that's -- in fact, we just had the international meeting in Boston, and that's the consensus.

DR. MC NEIL: Let's pretend it is. Can we pretend?

DR. DOMINITZ: The ASGE position is that they believe that these -- all lesions seen should be reported. And I understand the controversy around that. I understand why radiology wants to do it. But I think there is some contention about that issue.

DR. MC NEIL: On the radiology study or on the endoscopy study?

DR. DOMINITZ: The reporting of CTC findings. And I understand why radiology doesn't want to report them. And who know what'll happen in practice. The radiologists' societies recommend that you not report these lesions for the reasons Dr. Klein enumerated.

The ASGE position is that we feel that for the sense of openness with patients, whatever is seen should be discussed with the patient, and then decide what to do. We're not saying they you necessarily

would do a colonoscopy for these small lesions, but it might alter management.

DR. KLEIN: That's making the assumption that we can see these things. And what I'm saying to you is, make believe they're not there because it's not reliable.

So it's not that you say to a patient, look, I didn't want to tell you this, but there's a four millimeter polyp. You say to the patient -- and they get all this data ahead of time that says, polyps of this size cannot be reliably identified. Therefore, we make no promises about any polyp of five millimeters or less. That's just a limitation of the technology.

DR. MC NEIL: Wouldn't it be safe to say that we should assume that since the radiologists are reading it, and there seems to be some kind of consensus among the various groups that, in general, those results are not going to be reported for the purpose of answering this question?

And therefore, the GI doctor is -- or the

primary care doctor is going to be dealing only with six millimeters or more?

Thank you, Steve.

UNKNOWN MALE VOICE: (Unintelligible.)

DR. MC NEIL: Is that fair to --

UNKNOWN MALE VOICE: He's already written it down.

DR. MC NEIL: Okay. Is that reasonable to do? Okay. So then we're looking for CTC guidelines for referral for greater than or equal to six. Are there data -- is there sufficient evidence, rather?

Can we vote on that? We're voting just the polyp removal, 7-A.

UNKNOWN MALE VOICE: 7-A.

(Whereupon, the panel voted.)

DR. MC NEIL: Does anybody want to discuss 7-B?

DR. SINGH: 7-B? We have no evidence. We have no clue. We're struggling with guidelines that aren't colonoscopy (unintelligible) ten years and five years. And certainly for CTC we have no evidence how

frequently should we repeat it.

DR. MC NEIL: Sure, Steve.

DR. PEARSON: This may not be helpful. But I was going to say the evidence for frequency of screening doesn't exist for anything.

DR. SINGH: Exactly. Exactly.

DR. PEARSON: But what's interesting is I think the guidelines are appropriate because they're relatively conservative. You know, for CTC most of the -- what's talked about is doing it every five years. That's probably because sometimes there are going to be not biopsy-ing the six to nine millimeter lesions and watching them for a while.

My reading of the guidelines is that they have been appropriately conservative on the basis of a serious lack of evidence. So that's what's hard. I think there's not much evidence. But that they're appropriate. And that makes a difficult vote.

DR. SINGH: I think it's a different question. The question here is, is there evidence to make guidelines. That's one question. But what

you're saying is that the current guideline of rescreening every five years, is that appropriate.

The answer to the second question is, yes. The answer to the first question is, no. There is no evidence.

DR. MC NEIL: So there are two questions.

DR. SINGH: So those are two different questions.

DR. MC NEIL: We're going to just answer B.

DR. SINGH: It's B-1 and B-2.

DR. MC NEIL: No. We're going to just answer B.

DR. PHURROUGH: If the answer to the question is the guidelines are opinions are not evidence-based, that gives us a different level of freedom to evaluate the kinds of decisions we're going to make versus here's what we think the guidelines ought to be.

We're not looking for you to give us what your opinion is. We're looking for you to tell us what the evidence shows.

DR. MC NEIL: So that would mean 7-B would stay as it is.

DR. PHURROUGH: Stay as it is.

UNKNOWN MALE VOICE: Okay.

DR. MC NEIL: Can we vote?

(Whereupon, the panel voted.)

DR. MC NEIL: Well, easy and hard graders again. Our absentee colleague is an easy grader.

So let's see. What is the agenda now?

DR. SINGH: We're done.

DR. MC NEIL: We can have a final open panel discussion for an hour.

DR. SINGH: Shall we vote who wants that discussion?

DR. MC NEIL: Instead of doing that -- unless -- does anybody have a burning -- I'm going to ask -- we do have to do something with the panel members, but I think an open panel discussion for an hour is a bit much.

DR. MC DONOUGH: Were we going to ask anybody if they want to change their vote?

DR. MC NEIL: Oh, yes. Good idea, Bob.

Does anybody want to change his or her vote if you can

remember what your vote is?

DR. MORRIS: On number three, let's see, how confident are you the -- I can't remember why this later struck me as really problematic. I think it's because -- I should have written it down. I can't remember.

DR. MC NEIL: Well, while you're thinking, I guess at this point it would be useful it we would start off with Mike, if you have any comments about -- and you don't have to have. But if you do have any comments about why you voted for anything or didn't vote for anything.

MR. LACEY: Nothing additional. No.

DR. WEINER: Can I have a comment another way or just about the vote?

DR. MC NEIL: You can have any comment you want, Jonathan.

DR. WEINER: Then the comment is an obvious one, that I hope that if things are covered -- and

that's of course CMS's decision -- that it includes collection of evidence and data. Because one thing

that's clear is there's an awful lot of missing information.

DR. MC NEIL: How about Steve Teutsch? Does he have anything to say?

DR. WEINER: I could guess what he would say.

DR. MC NEIL: Can you give me proxy?

Okay. Why don't we just move along? Doctor Singh, anything to say about why you voted or didn't vote?

DR. SINGH: No. As I pointed out, I sort of read -- maybe I read the questions too literally. When the question said is there evidence, then I want to see evidence. And I didn't want to extrapolate evidence. So maybe that's why I voted the way I did.

DR. MC NEIL: Let's see. I can't see who's next.

UNKNOWN MALE VOICE: No. Nothing.

DR. PEDEN: I just -- I have one clarifying

sort of curiosity, actually, for Dr. Klein. You guys have said that you're not reporting less than five

centimeter lesions.

DR. MORRIS: Millimeter.

DR. PEDEN: Or five millimeter lesions. Sorry. Yeah. Why five as opposed to six, and does that create a dilemma between five and six? And is there a thought about what's supposed to be done there?

DR. KLEIN: You bring up -- Dr. McNeil, can I please use the microphone?

DR. MC NEIL: Yes, please. Yeah. The microphone would be better.

DR. KLEIN: Well, you bring up a great question because nobody except for you today has asked, how do we get these measurements? What's four millimeters, what's five millimeters, what's six millimeters, what's ten millimeters? Ten millimeters is the magic number.

Well, you know, does the gastroenterologist measure it in vivo, and how does that compare to the

pathologist's measurement when it comes out? And what about the radiologist's measurement on the CT or on

the three-D or the two-D?

So really, you know, these cut-offs are quite arbitrary. And in every single paper -- on every single paper that's ever been written about polyps, it arbitrary. It's not just this.

So the answer to your question is, I don't know nor does anybody else. A fifteen millimeter polyp is pretty much -- pretty clear versus a five millimeter polyp. But a five or a six or a ten versus a nine versus eleven -- you know, if it's nine or a ten, it's big difference according to our studies.

But quite frankly, if I measured it ten different times, some in a jar, some in the patient, some on a CT scan, they'd be all over the place. So it's a very legitimate question that nobody will be able to answer for you.

DR. MORRIS: I guess I answered three with the thought that we're not taking adherence into account at all. Was that correct? Because that might

20 really change things as well.

21 UNKNOWN MALE VOICE: (Unintelligible.)

DR. MORRIS: Okay. We decided that on a subsequent question, but just sort of retrograde.

DR. MC NEIL: Well, if you want to change your vote, you can.

Let's see. Bob?

DR. MC DONOUGH: I agree with Dr. Weiner about the need for perhaps some type of -- development of some type of data sets as a condition for coverage.

DR. GOODMAN: This is Cliff. Since any coverage decision is not going to be absolutely clear with perfect evidence, I have three plus two types of evidence just for the record that CMS may want to consider collecting, regardless of how the policy is written.

And some of this will sound familiar. Evidence for risks and benefits. You may want to consider collecting data on the radiation risks. And we know that that is going to be difficult to collect over a longer time frame. It can be done in part with

a registry and maybe model data, probably not RCT.

The second one is going to be risks and

benefits of extra-colonic findings. That may be done with a registry and maybe with controlled trials. Maybe an RCT could help collect that kind of data.

And those two echo a bit what Ned said.

The third one is data on -- as it unfolds, specificity of CTC for the six to ten millimeter polyp interval. There seems to be an important evidence gap there for the reasons that we discussed.

Then there are going to be two things to track. Two things to track are going to be adherence as it will affect costs. And I'm glad to hear that the model may be able to accommodate that.

So CMS already has paid for a model that can track how adherence -- it can track data on adherence that can be plugged into a model that will yield information about costs and cost-effectiveness. That will be very useful.

And then the final thing is, I hope that CMS can track practice patterns, particularly insofar as

different scenarios or hybrids of these procedures evolve. The data that we heard about today -- or the

models and scenarios about which we heard today are probably more simplistic with regard to use of CTC versus optical. And as time evolves, I think we're going to see hybrids.

And it will be very important for the Agency to see what happens in practice, and then use that new information as a kind of (unintelligible) and be able to plug that back into models and further considerations.

DR. PEARSON: Two thoughts. One is as a participant and long-time observer of this group, it's nice to be able to talk about cost-effectiveness. And I want to thank Ann and all the groups that put the effort into that because I think it does -- both just the modeling on the clinical effectiveness side for technology like this where we'll never have the right kinds of short term evidence.

I think it is very helpful for us to consider how robust the evidence is for effectiveness

through modeling. And I just want to applaud the work that you and the other groups did.

The other comment I had was just briefly about CED, which is a pet of mine. We would always love to have more data. I would just -- there are a few cautionary notes about this area in particular.

My fear is that CED -- the real information that we would be after here, as Dr. Calonge said, are things that we wouldn't be able to find out for perhaps years and years and years.

And so you just have to be very, very careful that you set up a mechanism that is at least realistic in terms of what you're going to find out eight to ten years down the road when we know that eight to ten years down the road, there will probably be a prep-less CTC.

There will be lots of other changes in the comparative opportunities. And maybe that the questions on the ground no longer really are driving the questions that we have here today.

So it's just a little bit of a cautionary

note while generally in favor of trying to learn as much as we can about such an important condition and

important set of alternative treatments or screening modalities.

DR. MC NEIL: So I have two comments. One is for the U.S. Preventive Services Task Force. And I thought your analysis was very good. What I'd like to see -- and I realize it's probably not possible, and it may not be applicable to everything that you do.

But in this particular example, I think it would have been great if in addition to the I, you indicated exactly what it would have taken to move off an I because I think might not have been possible to move.

For example, you mentioned radiation risk. And the issue there is cumulative risk, not the risk at any one point in time. So to determine, you know, that you went from 20 to 10 to 7 or 6 or whatever, that's probably not going to do a whole lot to help anybody model out the impact of radiation risk.

So just in general, it would be nice when

you put an I in for something like this, to figure out what exactly it would take to answer it. And you

might even want to do it for this one, to see what it would take with existing data sets to answer it. That's comment number one.

Comment number two is I am a little -- and this is -- I'm of two minds on this one. But I am a little concerned about collecting all kinds of mandated data sets by CMS, either under coverage with evidence development or just in terms of registries like carotid artery stints because all of those things cost money.

And I am worried that costs are going up. And somebody from Colorado said -- oh, I guess it was you, Ned. Every whatever, one percent increase was --

DR. CALONGE: 2500.

DR. BARTON: -- 2500 people uninsured. So I think we have to just watch out for that and make sure that when we say we want a data set, we really absolutely know that it's going to be totally unbiased. There's not going to be any selection as to

who gets in. There's going to be auditing on it.

That the cost of it is going to be reasonable or not.

And I am actually not sure that it applies in this situation. I almost thought that if you have or anybody has a CTC operation, they're going to have their own organization to track and compare their results with that of optical colonoscopy.

But maybe -- I would have thought any self-respecting group would do that, but maybe not.

So Ned, did you --

DR. CALONGE: I only want to say that we do include certain stats in our predication statement. And we did talk about the detection and subsequent evaluation of extra-colonic lesion.

I was sitting here being -- trying to be reflective of what if we had no concerns about extra-colonic and where we would put the radiation risk. And I think I don't know the answer to that since we had more than one concern on the harms side.

But it's a very interesting question that I even posed to Mary. I said I was wondering what we do

if that was the only concern.

DR. MC NEIL: I was actually saying

something slightly different. It's not --

DR. CALONGE: Oh, actually say what we would need to get off the I.

DR. MC NEIL: What would you need to get off the I? So it's one thing to say we've got these four percent serious extra-colonic concerns -- extra-colonic findings. The other is, how could we actually -- what patients, what sample size, what data set could ever give us the answer to that that would satisfy this group of pretty tough critics?

And that's what I was asking. It's easy to say, let's go look at some more data. Let's pull it out. That doesn't always work.

DR. GOODMAN: As I suggested collecting some of those data. I don't think it's necessary for CMS to say, we want some de novo registries.

But what CMS could suggest or request is that they would be interested in any research along those lines. They'd be interested if a Kaiser

Permanente or a VA or other large health systems with

centralized electronic medical records systems and

other large databases could be collecting -- could be analyzing these data for these kinds of questions.

So those I think would be fair to put forward without setting up brand spanking new registries.

DR. MC NEIL: Right. Steve? Sure.

DR. PEARSON: It just dawned on me. This is an easy request to those of you who are doing CTC now. Help us out because the incidental findings -- you can't help us that much with the radiation risk. But you know, try to build into your studies going forward everything possible to help us capture the boundaries around what's happening to patients with incidental findings.

Obviously, you're going to be working within your professional societies to come up with guidelines on how to report them. And hopefully, there are guidelines for what do with them after they're reported.

But it would just help so much if some of these really great studies that have been focused so

much on test performance included, you know, just that extra bit of effort to help us capture not just how many incidental findings, but what happens over the next six months to those patients. It would be great for us.

DR. PHURROUGH: Panel, thank you. It was a spirited discussion, the kind we like. And as typical at the end of these panels, there are a lot more questions. And that's why we have these panels. If they were easy issues, we wouldn't call you here to the room to discuss them.

So thank you for your time and efforts. For those of you who have not been part of this before, this is a challenging event for these individuals who are given lots of information to read and decipher. So there's some significant time involved in being part of this. And we appreciate your doing that.

And we really don't pay them much at all. We fly them here, and that's about it. So thank you

very much. And Barbara, I think we're done.

DR. MC NEIL: Yes. We're done. I just

wanted to thank everybody. I thought this was a great discussion among the panelists, and I thought the presenters and the audience did a great job. So bon voyage.

MS. ELLIS: Panel members, could you please make sure that I get your questions before you leave.

(Whereupon, the proceedings were concluded.)

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