CENTERS FOR MEDICARE AND MEDICAID SERVICES

Medicare Evidence Development & Coverage

Advisory Committee

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Centers for Medicare and Medicaid Services

7500 Security Boulevard

Baltimore, Maryland

Panelists

Chairperson

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Vice-Chair

Art Sedrakyan, MD, PhD

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CMS Liaison

Tamara Syrek Jensen, JD

Industry Representative

Martin D. Marciniak, MPP, PhD

Panelists (Continued)

Guest Panel Members

V. Paul Doria-Rose, DVM, PhD

Michael K. Gould, MD, MS

Jeffrey B. Rich, MD

Steven H. Woolf, MD, MPH

Invited Guest Speakers

Laurie Fenton Ambrose

Peter Bach, MD, MAPP

Doug Campos-Outcalt, MD, MPA

Paul Pinsky, MD

Executive Secretary

Maria Ellis

TABLE OF CONTENTS

Table of Contents (Continued)

PANEL PROCEEDINGS

(The meeting was called to order at 8:11 a.m., Wednesday, April 30, 2014.)

MS. ELLIS: Good morning and welcome, committee chairperson, vice chairperson, members and guests. I am Maria Ellis, the executive secretary for the Medicare Evidence Development and Coverage Advisory Committee, MedCAC. The committee is here today to discuss the use of low-dose computed tomography (LDCT) screening for lung cancer in adult smokers.

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 interests. Each member will be asked to disclose any financial conflicts of interest during their introduction.

We ask in the interest of fairness that all persons making statements or presentations disclose if you or any member of your immediate family owns stock or has another

formal financial interest in any company, including an Internet or e-commerce organization, that develops, manufactures, distributes and/or markets, consulting, evidence reviews or analyses, or other services related to LDCT screening for lung cancer. 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 this room.

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. We ask that all speakers addressing the panel please speak directly into the mic and state your name.

For the record, voting members present

for today's meeting are Dr. Art Sedrakyan, Dr. Harry Burke, Dr. A. Mark Fendrick, Dr. Mark Grant, Dr. Jo Carol Hiatt, Dr. David Howard, Gail Melkus, Dr. Gail Melkus, Dr. Curtis Mock, and Dr. Gerald White, Jr. A quorum is present and no one has been recused because of conflicts of interest.

The entire panel, including nonvoting members, will participate in the voting. The voting results shall be available on our website following the meeting.

I ask that all panel members please speak directly into the mics, and you may have to move the mics since we do have to share.

This meeting is being webcast via CMS

in addition to the transcriptionist. By your attendance, you are giving consent to the use and distribution of your name, likeliness and voice during this meeting. You are also giving consent to the use and distribution of any personally identifiable information that you or others may disclose during today's meeting. Please do not disclose personal health information.

In the spirit of the Federal Advisory

Committee Act and the Government in the Sunshine Act, we ask that the advisory committee members take care that their conversations about the topic at hand take place in the open forum of the meeting. We are aware that members of the audience, including the media, are anxious to speak with the panel about these proceedings. However, CMS and the committee will refrain from discussing the details of this meeting with the media until its conclusion. Also, the committee is reminded to please refrain from discussing the meeting topic during breaks or lunch.

If you require a taxicab, there are

telephone numbers to local cab companies at the desk outside of the auditorium. Please remember to discard your trash in the trash cans located outside of the room. And lastly, all CMS guests attending today's MedCAC meeting are only permitted in the following areas of CMS single site: The main lobby, the auditorium, the lower level lobby, and the cafeteria. Any persons found in any area other than those mentioned will be asked to leave the conference and will not be allowed back on CMS

property again.

And now, I would like to turn the meeting over to Tamara Syrek Jensen.

MS. JENSEN: Thank you, Maria. I know we have a packed agenda today so I'm going to keep it very short. I just want to thank everyone for coming to the MedCAC today, this is an important meeting for us.

As many of you know, we have an open national coverage determination going on right now and this is part of our information collection to use to make a decision on this particular topic, which will be due in mid

November, so our national coverage determination proposed decision is due in mid November, where everyone can then have another 30-day public comment on that proposed decision, and then we will issue a final 90 days after the proposed has been made public. And we haven't missed any statutory due dates so I think you can expect those dates to be met, so look for that decision in that time.

So, this is a very important meeting to us for that decision, and we will be using the information in this meeting to help us make

that decision. This meeting is about the evidence and what this panel thinks of the evidence, and so we're very excited to hear from all of you and our panel. I just want to remind you that I know today's meeting is very very structured, and Rita and Art are going to have a very hard job of time-managing the entire meeting, so please don't be offended if they say you only have ten seconds. If you have not finished what you need to tell us, please give it to us in writing, we will take it under advisement, but we do need to get the

meeting, everybody to have a chance in the meeting, and that is why there are certain time constraints on there, and we do depend on Rita and Art making sure that those time constraints are met today.

So again, thank you to all of you for showing up today, and a very special thanks to the MedCAC members for coming here today, and now I'm going to turn it over to Rita Redberg.

DR. REDBERG: Thanks very much, and I just want to add my welcome to Maria's and Tamara's to everyone here, as well as the committee. We really appreciate everyone's

service and interest in this important question we have before us today.

We will just start out, I will introduce myself and then we'll go down the line and everyone will introduce themselves.

I am Rita Redberg, I'm a professor of medicine at the University of California, San Francisco, I'm also a cardiologist there. I am also the editor of the JAMA Internal Medicine. I have no conflicts of interest.

I did write an op-ed in the New York

Times in January called We're Giving Ourselves Cancer, that concerns the excess cancers that are occurring in the US from radiation risks, and we discussed ways to decrease radiation risks leading to cancer in the US. I had no knowledge of the MedCAC meeting and we were not specifically addressing lung cancer screening, but we did talk about CT scans.

Similarly, in the journal I edit we have a series called Less is More, where we do discuss harms as well as benefits of new technology, and we talk in specifics about how to weigh harms and benefits of those technologies. I'm here on my own behalf and

not representing the journal.

DR. SEDRAKYAN: I'm Art Sedrakyan, I'm an associate professor at Weill Cornell Medical College. I am directing a patient-centered comparative effectiveness research program focusing on devices and surgical interventions, and I don't have any conflicts related to this MedCAC.

DR. FENDRICK: Good morning. Mark Fendrick, general internist. I direct the

Center for Value-Based Insurance Design at the University of Michigan. No conflicts.

DR. BURKE: Hi, Harry Burke, associate professor in biomedical informatics and medicine, uniform services, University of the Health Sciences. I have no conflicts of interest and I represent the federal government.

DR. GRANT: I'm Mark Grant, I'm the director of technology assessments at the Center for Clinical Effectiveness, Blue Cross Blue Shield Association. I obviously work for an insurer which does cover Medicare beneficiaries, but I'm here on my own behalf and have no conflicts of interest.

DR. HIATT: Good morning, I'm Jo Carol Hiatt, I chair the Inter-Regional New Technology Committee with Kaiser Permanente, and I'm also here on my own behalf with no conflicts, and I'm a general surgeon.

DR. HOWARD: I'm David Howard, I'm a faculty member at the Rollins School of Public Health and Winship Cancer Center at Emory University, and have no conflicts of interest.

DR. MELKUS: Good morning, I'm Gail D'Eramo Melkus, and I'm professor of nursing at the NYU College of Nursing and associate dean for research. I'm also a certified adult nurse practitioner and a fellow in the American Academy of Nursing, and I have no conflicts.

DR. MOCK: I'm Curtis Mock, certified in internal medicine and geriatrics, serving as the national medical director for complex population management with Optimum Health. I'm here on my own behalf as a patient advocate and I have no conflicts.

MR. WHITE: I'm Gerry White, I'm a clinical medical physicist in Colorado Springs and I have no conflicts.

DR. MARCINIAK: I'm Martin Marciniak,

I am the vice president for US health outcomes and medical policy for GlaxoSmithKline. I'm also the industry rep.

DR. DORIA-ROSE: I'm Paul Doria-Rose, I'm an epidemiologist at the National Cancer Institute. I'm here on my own behalf today and I have no conflicts.

DR. GOULD: Michael Gould, I'm a

pulmonologist and health services researcher. I direct the program in health services research in the department of research and evaluation at Kaiser Permanente Southern California. I have written fairly extensively about pulmonary nodule evaluation in lung cancer screening, served as a member of the multi-society task force for lung cancer screening guidelines sponsored by the American College of Chest Physicians and the American Society of Clinical Oncology, and I've received salary support from Archimedes to help develop computer modeled lung cancer screening.

DR. RICH: I'm Jeff Rich, I'm a practicing cardiac surgeon and chief of cardiac surgery at Centura Health Care. I do not do thoracic surgery, so I have no conflicts with

regard to any decision made here. I'm past president of the Society of Thoracic Surgeons but I don't have a leadership role in that society anymore, but I have been very sensitive to these issues for the membership of our society, and I'm here representing myself.

DR. WOOLF: Steve Woolf, professor of

family medicine and population health at Virginia Commonwealth University. No conflicts of interest to report. I do have a long history with the U.S. Preventive Services Task Force, 16 years, both as a staff member, later as a member of the task force, and ultimately the senior advisor to the task force. It was many years ago when the primary screening test was chest x-rays, and I have not been involved with the task force for about ten years, and was not involved with the current recommendation we're deliberating on.

DR. REDBERG: Okay, thank you all, and with that I would like to introduce our first speaker, Dr. Joseph Chin, who will present the CMS presentation as well as the voting questions.

DR. CHIN: Good morning. I'm Joseph

Chin, I'm in the Coverage and Analysis Group and the lead medical officer for this topic today, screening for lung cancer with low-dose computed tomography in adult smokers. I will be presenting some basic background about lung cancer screening and also about how Medicare

considers preventative services statutorily is different than evaluation and management services. I will also read the voting questions for the record.

Cancer of the lung and bronchus is the third most common category of cancer as estimated in 2013 by the National Cancer Institute, this is from their website, SEER data. In 2013 there was over 200,000 new cases estimated, accounting for 159,000 deaths. The NCI recently, you know, sort of posted estimates for 2014. The numbers and relative rankings are consistent with the 2013 numbers.

New cases of lung cancer and bronchus cancer, the majority of new cases, as you can see from the graph here, occurs in older adults, 65 years old and older, accounting for 68 percent of new cases, median age at diagnosis at 70 years, and again, the 2014

estimates from NCI were similar. Deaths from lung cancer also occurs largely in adults over 65 years of age. Basically this category, you know, accounts for about 70 percent of all deaths in the older age group, median age at 72

years. So with the number of new estimated cases and also the estimated deaths, there is a disproportionate share in older adults, essentially the Medicare population.

Also, another slide from the NCI SEER website looks at stage of diagnosis and survival, and unfortunately for lung cancer, most of these cases are diagnosed at a pretty late stage, with distant metastases, which is, you know, associated with a relatively poor five-year survival rate. So in that sense, if there were a suitable test to diagnose, to early detect this condition, you know, for example in the localized stage, there is some possibility for improving the five-year relative survival.

The number of risk factors for lung cancer, also again from the NCI website, we will be focusing on the first one, smoking cessation, cigarette smoking and tobacco use,

now and in the past. These other ones are important; however, we won't be discussing them today.

We can get a sense of smoking status

in the Medicare population by looking at the Medicare Current Beneficiary Survey, which is a longstanding representative survey of the Medicare population. In 2011, 14 percent of respondents were current smokers, and 44 were former smokers. This pattern has basically been pretty consistent over the years. The figure at the bottom here shows over the past ten years, and there has been little change in the reported smoking status in the Medicare population. Unfortunately in the current survey, there is no question about smoking history or cumulative smoking risks.

So, lung cancer screening has actually been a consideration for many years, dating back to the 1960s and '70s, actually as Dr. Woolf mentioned. In that time period there was really, it started off with, you know, sputum technology and chest x-ray, or a combination, and none of those approaches really panned out. Screening studies with, you know, low-dose CT,

actually gained attention probably in the late '90s, and even the early studies on LDCT screening did not conclusively show mortality

benefits until 2011 when the results of the National Lung Screening Trial were published, which actually showed that screening with three annual low-dose CTs reduced mortality from lung cancer compared to chest x-rays in adults 55 to 74 years of age, who had at least a 30 pack-year history. This is the publication that came out.

The next two slides will go over basically how CMS and Medicare considers preventive services, and historically when Medicare was established in 1965, it was to pay for items or services that, you know, were -- that are reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member. This basic language had generally included preventive services.

Medicare does cover a number of preventive services, starting back in 1997 with the Balanced Budget Act. In 2008 CMS did receive authority through the Secretary of HHS

to add additional preventive services in the Medicare Improvements for Patients and

Providers Act, we refer to it as MIPPA. Section 101, improvements to coverage of preventive services, which lays out the criteria that CMS considers to add additional preventive services, all these criteria need to be met: Reasonable and necessary for prevention or early detection of illness or disability; recommended with a grade A or grade B by the U.S. Preventive Services Task Force; and appropriate for individuals entitled to benefits under Medicare Part A or enrolled under Medicare Part B.

So, the USPSTF recommendations are important to our considerations, it's one of the three criteria that are necessary, not sufficient by itself. For those that may not be familiar, the USPSTF is an independent panel of nonfederal experts in prevention and evidence-based medicine, and it conducts scientific evidence reviews over a broad range of clinical practices and health care services such as screening, counseling and preventive medications, and developing recommendations for

primary care clinicians, and this

recommendation is taken directly from their website. The Agency for Healthcare Research and Quality, AHRQ, provides the administrative and operational support for that task force.

So, the task force has looked at lung cancer screening several times, and their first recommendation in 1985 was a Z, so the course of their recommendations have paralleled the developments in the evidence. In 2004 the recommendation was changed to an I, and the end of last year, 2013, the USPSTF revised their recommendation to a grade B, here, for annual screening for lung cancer with low-dose computed tomography in those aged 55 to 80 years who have a 30 pack-year history and currently smoke, or have quit within the past 15 years.

This is a fairly complex recommendation, there's a number of considerations to look at, especially for implementation. You know, for example, to accurately ascertain smoking history, which is most commonly self-reported, that's, you know, really a factor that may influence the risks

and benefits actually in a screening program outside of specific, you know, clinically controlled trials.

The NLST investigation also noted a number of implementation issues in their publication. They basically focused on the expertise in radiology in the diagnosis and treatment of cancer in their participating medical centers of the trial, which may or may not, as we mentioned here, be available in some of the community facilities.

So, on to the voting questions. Voting question one, how confident are you that there is adequate evidence to determine if the benefits outweigh the harms of lung cancer screening with LDCT (CT acquisition variables set to reduce exposure to an average effective dose of 1.5 millisieverts) in the Medicare population?

If at least intermediate confidence, score greater than or equal to 2.5, A, how confident are you that there is adequate evidence to determine that screening in asymptomatic high risk adults over 74 years of age improves health outcomes? B, how confident

are you that there is adequate evidence to determine that annual screening beyond three annual LDCT screenings improves health outcomes? And C, how confident are you that there is adequate evidence to determine that a lung cancer screening program implemented outside a clinical trial improves health outcomes?

Voting question number two, how confident are you that the harms of lung cancer screening with LDCT (average effective radiation dose of 1.5 millisieverts) if implemented in the Medicare population will be minimized?

And the discussion question related to that, what harms are likely to be relevant in the Medicare population, including, (a), harms from the LDCT itself; (b), harms from follow-up diagnostic evaluation of findings in the lungs and incidental findings outside the lungs; and (c), harms from treatment arising from positive and false positive results? What provider and facility criteria or protocols are helpful in minimizing harms?

The last voting question, voting

question number three, how confident are you that clinically significant evidence gaps remain regarding the use of LDCT (average effective dose of 1.5 millisieverts) for lung cancer screening in the Medicare population outside a clinical trial?

And the discussion question with that is, if there is at least intermediate confidence, score greater than or equal to 2.5, please discuss any significant gaps identified and how CMS might support to their closure.

Thank you very much.

DR. REDBERG: Thank you, Dr. Chin.

DR. CHIN: There is some additional discussion questions, so I should read them.

Please discuss whether these or other topics should be considered for further research in the beneficiary population. If yes, why? (i), risk factors/criteria for eligibility of screening asymptomatic individuals; frequency and duration of testing; what impact will adherence have on lung cancer detection (National Lung Screening Trial adherence was 95 percent); definition of a positive screen and variability of false

positives and how false positives should be resolved; the rate, classification and standard evaluation of incidental findings; and impact of lung cancer screening on smoking cessation rates.

DR. REDBERG: Okay. Thanks very much, Dr. Chin, that was a great presentation for the background of our evidence today, as well as the voting questions and the discussion questions. And I will also note that even with the backup slides, you finished before your allotted time and set a great example for the rest of the morning.

So, the next speaker is Dr. Paul Pinsky, who's from the Division of Cancer Prevention at the National Cancer Institute at the National Institutes of Health, and Dr. Pinsky, you have 20 minutes.

DR. PINSKY: Thank you. So, Dr. Chin mentioned the NLST or National Lung Screening Trial and briefly some of the design and findings, but I'm going to go into, you know, some detail of the design of the trial and the findings, and also try to emphasize some points

related to dissemination into the population

setting. I do not have any conflicts of interest.

So, the basic design of NLST was a randomized trial where subjects were randomized to either low-dose CT or chest radiograph over three annual rounds of screening, with a total followup of six to seven years, so about three to four years after the last screen they were continued to be followed.

The issue of the diagnostic followup of positive screens is important and relevant for how it would translate into a population setting, so we did not have a trial-wide algorithm for diagnostic followup in NLST. The study radiologists did give recommendations based on their clinical judgment, but overall the diagnostic followup, as well as treatment, was conducted outside of the auspices of the NLST.

The primary outcome was lung cancer-specific mortality, and secondary outcomes of all-cause mortality, lung cancer incidence and stage distribution.

The eligibility criteria, which the last speaker mentioned briefly, basically

30-plus pack-years of cigarette smoking, and being a current smoker of having quit within 15 years, and then age, 55 to 74, those were the major criteria, along with some others.

It's interesting to see how those criteria played out in terms of the actual NLST trial population, so we see roughly half were current smokers and half former smokers, and that's the distribution of time since quit. The median pack-year is 48, and in the 25th to 75th percentile there, 39 to 56, so the majority of subjects had well more than the 30 pack-year minimum, so 75 percent had at least 39 pack-years.

It's very relevant for this discussion what the age distribution was, so in NLST, 25 percent were 65-plus Medicare age.

Now it's also of interest to compare the NLST population to an estimate of, for the whole U.S., what the NLST eligible population would be. So we, NLST is a little bit underrepresented in terms of current smokers,

median pack-years was similar, and it was also younger than the overall U.S. population that would meet the NLST eligibility criteria, so

overall in the U.S. it would be about 35 percent would be 65-plus.

The radiologist requirements were board certified, fairly standard. The last bullet there, we did come up with a dedicated NLST training set of images that all of the NLST radiologists had to look at before the trial.

In terms of the CT settings for the NLST protocol, a kVp 120 to 140, mAs 40 to 80 depending on participant body size, and other parameters. There was a study of the, trying to estimate what the effect of radiation dose was in NLST, and this was based on the estimated radiation dose using techniques to image the average sized person in NLST, so this is basically, essentially based on an mAs of about 40, and we see an average effective dose of 1.4 millisieverts. Now in practice, about 25 percent of the time the mAs was 70 or greater in NLST due to larger patients, so this

1.4 is probably a little underestimate of the average actual effective dose among NLST subjects, but it could be a little higher.

So, moving on to the actual screening,

a very important point is what the definition of a positive screen was. So the basic definition was a noncalcified nodule that had a maximum diameter of at least four millimeters. Other suspicious findings could also result in a positive screen, but the bullet at the bottom there shows that 98 percent of positive screens did have at least one four-millimeter nodule, so that was essentially what the definition was.

Another important point, especially for translating into the population setting, is that of the final third-year final screen, that an NCN that was stable for two years could be classified as a negative result at the discretion of the radiologist and as you'll see, that affected the positivity and the false positivity rate on that final screen.

So now I'm going to go into the major NLST results, starting with the screen

adherence and positivity, diagnostic followup for positive screens, and then lung cancer incidence and stage, mortality, primary outcome, both lung cancer-specific and all-cause mortality as secondary outcome, and

some screening center and radiologist factors, and finally results stratified by age, 65-plus or less than 65, which is very relevant to this discussion.

So, at the bottom there you see the overall adherence to LDCT screening was very high, at 95 percent. In terms of the screen positivity, it was 27 percent at baseline and roughly the same at year one, but it's of interest that at year one, over half of the positive screens actually were positive screen with no significant change. So that means that the nodule was stable and did not change from the T-0 to the T-1 screen in the estimation of the radiologist, and there were no new nodules.

Now at the year two screen where the radiologist had the discretion to not call a stable nodule as a positive screen, there was a substantial decrease in the positivity rate to

16.8 percent, but even there over half of the screens actually did not have a significant change, and that's because the radiologists had the discretion whether to call it positive or not, and some still wanted to call it a positive screen.

But this is relevant because in a population setting at a steady state, most people would have a two-year history of screening, and you would have the option of assessing stability most of the time in the population setting as opposed to the trial.

In terms of the diagnostic followup of positive screens, it was separated into the baseline and year one and two screens because there was differential patterns, so at the baseline screen 90 percent had some sort of diagnostic followup, and about three-quarters had a chest CT as part of the diagnostic followup.

Invasive procedures, especially in subjects found not to have cancer, were quite low, at about 3.7 percent there, and surgical procedures even rarer, at 1.3 percent.

Moving to the year one and two screens, there was a lower percentage that had any diagnostic followup, a lower percentage that had chest CT, only about, a little more than a third, 34 percent, and that was largely because a lot of the positive screens in years one and two had a positive screen with no

change in the nodule, essentially a stable nodule.

Moving on to the positive predictive value, it was about four percent at each screening period, and some people may have heard this figure, that 96 percent false positive rate, and that's basically one minus the PPV. If you look at the prior positivity rates of 27 percent there, since 96 percent of those were actually false positives, the false positive rate is essentially the same as the positive rate, so quite a high false positive rate, especially at the first and second screen.

Finally, if we look at the last line, which is complications of diagnostic followup, and looking at those with no cancer, the rate

is fairly low, at .3 to .4 percent.

So let's look at the outcome, one of the secondary outcomes, which was lung cancer incidence and stage. There was a small excess of diagnosed cancers in the CT arm, quite a large excess of screen-detected cancers, over twice as many screen-detected cancers in the CT arm, and when you go to Stage I lung cancers,

again, there's a large increase in Stage I cancers and screen-detected Stage I cancers in the CT arm.

Also important is that there's an absolute decrease in Stage III and IV cancers in the CT arm, so about a little over a hundred fewer Stage III and IV cancers in the CT arm.

And an important issue in terms of the harms of screening, in addition to false positives, is over-diagnosis, and in a randomized trial setting, one way to quantify over-diagnosis is the excess CT arm cancers as a fraction of the screen-detected cancers by CT, so there was 119 excess cancers in the CT arm, and out of the 649 screen-detected cancers that's 18 percent, so we report an

over-diagnosis rate of 18 percent defined in that way.

The lung cancer-specific mortality, these were the rates. The figure that most folks are familiar with is the relative risk of .80, which is equivalent to a 20 percent mortality benefit. That was reported in the New England Journal paper in 2011. The end of followup was December 31st, 2009. For the

paper in terms of lung cancer mortality but not overall mortality, we used the January 15th deadline to be able to do all the endpoint verification, which certifies the cause of death. So when we use all data through December 31st when we had time to do all the endpoint verification, there's a little difference in the rate ratio there. The number needed to screen was similar, though, and again, the number needed to screen is defined as the number needed to screen to prevent one lung cancer death.

All-cause mortality, we actually found a significant reduction in total deaths or all-cause mortality. The rate ratio there is

equivalent to a 6.7 percent mortality decline. It's actually very rare in a screening trial to find a significant difference in all-cause mortality. In NLST we had a very high risk population for a very high risk cancer, so that was the major reason, a fairly high percentage of all the deaths were from lung cancer, so if we exclude lung cancer deaths, there was no significant all-cause mortality, or other cause mortalities decline.

So, I want to move now a little bit to some of the center and radiologist factors. So, one interesting thing which I think would have implications for dissemination to the population was extreme variability in radiologists' false positive rates. There's always variability in image interpretation but this might be more than, say, for mammography or other modalities. So we see that among 112 NLST radiologists who had at least 100 CT interpretations, there were some who had a false positive rate of ten percent or lower, and others who were up at 50 percent or higher, so a very large variability.

This, as I mentioned in part of the design, the radiologists made recommendations for followup of positive screens, so if we look at the baseline positive screen stratified by nodule size, you see there's a fair amount of variability in the radiologists' recommendations. So this is just to emphasize that there was no standard algorithm that the radiologists had to use to say four to six-millimeter, you had to recommend, you know, one specific thing, there was a variety across

radiologists, to some extent within radiologists, even within the strata, about what the diagnostic followup should be.

Another issue which was very important in terms of translating to a population setting is the idea that NLST was carried out in nonrepresentative settings, academic settings primarily, so it's a little bit of a judgment call whether a site is called academic or not, but we made a judgment, and by that most of the centers were academic, but the nonacademic sites tended to be larger size, so in terms of percentage of subjects, a little over a third

of subjects actually were screened at the nonacademic sites.

If you look at specificity and sensitivity, they're similar between academic and nonacademic, a little higher specificity in one, a little higher sensitivity in the other. But a very important point is this is just the screening per se, so for screening to be effective, obviously you have to have diagnostic followup, you have to have good treatment. So the diagnostic followup and treatment, even at an academic site, was not

necessarily carried out at that center.

We did not collect rigorous information on this for the trial, but anecdotally at least for a lot of the academic centers, we estimate that the majority of the diagnostic followup was not done at that center, but it was done at a patient's local community facilities. That's an important point to think about.

So finally, getting to results by age which, you know, is an important discussion here, there were some differences, fairly

minor. Adherence was high in each age group, a little higher positive screen rate in the older population.

Something which I didn't mention before is this idea of significant abnormalities that are not related to suspicion of lung cancer, and that's going to be an issue going forward, how to deal with these non-lung abnormalities, but in terms of significant abnormalities, again, it might be just a little higher in the older population.

The positive predictive value was higher, and this is in large part due to the

higher incidence rate in the older age group.

Complications were not significantly different.

Finally, if you look at the ratio for lung cancer and all-cause mortality, there was no significant difference by age.

So, I just want to spend the last minutes discussing my take on one of the questions that dealt with extending to greater than three screens that we saw at NLST. So, some arguments in favor of extending it beyond

the three annual screens in terms of population screening, trial screening scenarios, including NLST, are usually based on logistics of the trial, how to do the trial as quickly and inexpensively as possible, and they're not intended to be the basis of a population regimen. So it was never intended that because NLST was three screens, that that would be necessarily what would be recommended should the trial be successful.

But again with mammography, when Medicare coverage was introduced, there were a number of trials, but I don't think any had more than five or six screening rounds, even

though mammography is done over 20 or 25 screening rounds.

There's a problem with tracking CT screens prior to Medicare entry, so they wouldn't know if you had had a number of prior screens.

The harms, false positives, radiation can in large part, or at least some part be projected from the shorter screening regimens, and modeling efforts have attempted to

extrapolate benefits to longer-term screening, and there was one prominent modeling effort that accompanied the task force guidelines in the Annals, that extrapolated to a population screening setting.

There are some caveats, though. One, the NLST was one-third prevalence screening, meaning the baseline screen, and long-term population screening would primarily be repeat screening, so there might be different outcomes.

And NLST, as I mentioned before, had only one of three rounds with a two-year nodule history where you could judge a stable nodule, and in population screens you generally have

that history, so you may have the potential of revisiting the false positive rate because a lots of these nodules would be stable.

And the models that extrapolate benefits and harms, of course must be viewed with caution, as with all models.

And long-term adherence to screening, adherence was very high in NLST, but the long-term adherence in the general population

is unknown.

Thank you.

(Applause.)

DR. REDBERG: Thanks very much, Dr. Pinsky. And our next speaker is Dr. Peter Bach, who is an attending physician and director of the Center for Health Policy and outcomes at Memorial Sloan-Kettering.

I will just note that we will be taking questions and answers later on in the session.

DR. BACH: Great. Thanks, Rita, and thank you very much for having me, I'm excited to be here. I have been working in this field for a while, and I'm here to request that the MedCAC consider the evidence, and that CMS

consider covering LDCT in the Medicare population.

I've asked for a couple of provisions, that it be done in places with a certain level of expertise, sort of a TBD, what that constitutes. That a registry be put in place so that some of the unanswered questions that could be answered in an observational context

are. That there is a qualification of sites that include informed decision-making as well. So those are sort of the parameters. I think there's an opportunity to do this right. It's a promising technology with both high costs and high risks, but I also feel if we don't do it right now, it's a genie that certainly won't be able to be stuffed back into the bottle.

I have no financial conflicts of interest. I was the lead at three separate guidelines, including the multi-society guideline that Mike Gould mentioned. I am a member of the MedCAC, I'm here on my own today, and I'm going to discuss off-label use of the CT scan, as the CT scan or CT scanner is only labeled for clinical use.

A number of the issues have been

addressed by Paul already, I'm going to talk about extrapolating the evidence from the NLST in the following domains. I'm also going to talk, if you look at the bottom, about harm minimization opportunities, and about individualized decision-making in the context of large risk variation.

The basic questions of extrapolation, Paul has touched on them to some extent, was this group study generalizable, are the findings in terms of mortality, false positives and adherence generalizable, were the settings generalizable, and some basic questions of things that we can't even know enough to know if they are generalizable.

As Paul noted, the NLST showed in a highly regulated randomized trial a reduction in the deaths from lung cancer in people having low-dose CT relative to chest x-ray, as shown on this slide. It had, as Paul noted, partial overlap with the population that would have been in the study had it been randomly sampled from people with the same risk factors the NLST included. As Paul noted, it underrepresented people particularly in the older age band, they

randomly sampled people, they had a 14 percent study sample between the 70 and 74 age band, and they came in at about nine percent, and as Paul already noted, only about 25 percent of the NLST study subjects were in the Medicare eligible age group.

It also had an overeducated population relative to the tobacco using populations as a whole. Both of those things, I would speculate, would tend to make CT screening look more efficacious and less harmful than if the direct population had been representative.

If you contemplate the impact or the role of NLST and as it overlaps the population of people dying of lung cancer, you can see on this slide there is, again, partial overlap. The blue histogram represents deaths from lung cancer by age at death in the chest x-ray arm, essentially the observational arm of the NLST. The red histogram shows deaths from lung cancer in the SEER data in the U.S., so partial overlap. Lung cancer is primarily a disease of the elderly, NLST was primarily a study of somewhat younger people.

Paul noted this as well. The care

settings are not typical. I concede the point certainly that much of the care spread from these academic centers, many of which were NCI designated, into the community, and that's a terrific thing that we'll learn more about as

we study the NLST data. But nevertheless, these are the sorts of settings that have particular expertise. I think we have at least two decades of research demonstrating that care in centers like these is both less harmful and more efficacious, leading to questions about extrapolation to the community.

Paul showed a nice slide at the radiologist level from the NLST.

This is a slide looking at the false positive rates of all the published studies from our recent JAMA article, in the top is the RCTs and the bottom is the observational arms. False positive rates vary, as do the lung cancer detection rates shown in the dark part of each of these bars. The pooled data of these represents about 20 percent of false positive rates, that's just one number that really does depend on care setting.

This is the clinical problem. 19 CTs

of 20 has a false positive, one has lung cancer, that's the average I just showed you on the prior slide. I won't pimp anyone, although I'm looking at Mike Gould, who probably has a

sense of which one is cancer here, but nevertheless, it illustrates the basic problem. This is the cancer. Everyone else is potentially harmed.

The rates of follow-up procedures and invasive procedures for lung cancer are also inconsistent across the study. There is good news on this slide as well. If you look at the bar charts when biopsies are performed and there's a black area, that means it was found malignant, the gray area means intervention for things that ended up not being cancer, essentially another source of harm. Please note that the X axis only stops at eight percent here, so these are not high rates, they're single digit rates.

You'll see this in another slide deck as well. There are actually four randomized trials shown above the NLST in this table, are three smaller trials. These trials have weaknesses, they're all in the evidence review.

They had smaller sample size, they did inconsistent followup, there's actually some data ascertainment problems as well. But

nevertheless, the NLST result has not been reproduced in three other randomized trials in terms of lung cancer mortality reduction. That is not the case in terms of the effective cause of death on other causes than lung cancer, Paul correctly reported that the NLST reduced overall causes of death, but that was purely from mediation reduction death from lung cancer. If you look at the rate of death from causes other than lung cancer in the NLST and these other four studies, there is no evidence that CT screening reduces the rate of death from anything like cardiac disease or any other cause.

We know little about the incidental findings. Paul again alluded to this. This is a graph from the Lahey Clinic, which I think their study is ongoing and you'll hear more about. This is just a pie chart of all the other stuff that is found from CT screening. We don't know if these findings are incidental, ultimately leading to harm, really a great

opportunity to improve outcome, or anything in between. We need to understand this better.

As I noted, we do know that none of these studies showed an overall reduction in death from causes other than lung cancer, and these might be such things.

Adherence, as Paul noted, is inconsistent but was high in the NLST.

And then we have some important questions. What to do where we don't have data. What about unstudied groups, what about unstudied durations? We don't have data constraining over 74, and in fact NLST is underpowered in the over 65 group. We don't have data for longer duration. We don't have data for real world settings. What can we infer, and can we trust our models?

As I noted, the age band in NLST is low with respect to the population that's both recommended by the USPSTF and the Medicare eligible population. Fewer than 12 percent of subjects over age 70, and it's actually nine percent.

There's something good about going on to older ages. The risk of lung cancer rises;

shown here are two prototypical patients,

somebody who's 80 with a 50 pack-year smoking history, has about an 11-time greater risk of death from lung cancer than somebody who would barely be eligible for NLST eligibility criteria, a 55-year-old with 30 pack-years.

But there are bad things too that happen with advancing age in terms of the net benefit tradeoff. Rising risks of false positives, life expectancy reductions, and risk of surgical death, all three of those things are shown empirically on this slide. These are the three bad trends, if you will, as you go from the advanced age in terms of the net benefit tradeoff. The blue line shows a declining probability or declining life expectancy by age for smokers that's based on system models for smokers, not for people with lung cancer but for smokers with any smoking history. If the NLST population was skewed even older, you would expect that it would be marginally lower.

The rising orange line shows the false positive rate. This is from the NLST data, this is an analysis we did by age, we've

extrapolated beyond the NLST data. Extrapolation or not, that's the dashed line that doesn't matter, the point is obvious, the harms that are related to false positives will rise with advancing age. And then shown in the yellow is data and back extrapolation from SEER Medicare data, 30-day mortality in SEER from low back or sub low back for Stage I-II non-small cell lung cancer. As people age, unfortunately their risks from surgery rise, and even mortality at 30 days rises.

There's some question about longer duration. We are dependent on models to look at this, and from the CISNET group I've taken the view, and I wrote one of the two editorials that went with the CISNET paper in the task force, but the CISNET models probably are not adequate to determine what will happen over a long period of time with screening. It's not out of disrespect, it's just an empiric observation.

The basic argument is there were five separate modeling groups, those groups each produced estimates, and they matched so poorly to one another that I think we're left

wondering, are any of these right, but for sure four of the five have to be wrong because they're not overlapped.

And the variation of what these models produced was extremely wide. One model, for example, per 100,000 people were estimated 2,000 life years gained in the population, another 5X that. One model in terms of over-diagnosis estimated about 72 people, another five or six times that. These models because they don't agree probably can't be relied on.

And they also don't mimic, the first test of a model, it doesn't mimic what you can actually observe in real nature, and they don't.

Here's a figure from the AHRQ technical report of the CISNET model. Shown on the black graph is the cumulative risk ratio of deaths from lung cancer in the CT arm versus chest x-ray arm or, pardon me, other way around, chest x-ray versus CT, so it's greater than one over time. It's cumulative. You will see an immediate effect of CT screening, more deaths in the chest x-ray arm, and then this

smooth plot. All of these other dots, X's, et cetera, are the different models. You will note that at the beginning they don't match, they didn't hit the target.

You might look at this and say oh, well, by six years, at the end, they did, so we should all be comfortable that if we extrapolate further, we're good, note this. The problem with that is it's clear in the technical report that these models were all post hoc recalibrated to match at six years. I'm unable to find, and this is not a critique of the methods, please don't misunderstand me, I'm unable to find to what extent these things had to be recalibrated, but if you don't hit the targets, that means you can't trust the data going forward.

In terms of harm minimization there's some important good stuff going on, there's numerous efforts to codify approaches to false positives, the LungRADS you'll hear about. There's efforts underway to create standards but there's also some mis, if you will, some misdirection. Statements that we can reduce false positives I think are plagued with some

problems, and there's also trusted lists of screening sites which, to be honest, I think can't be trusted.

In terms of the reduction of false positives, I just want to note that there's a recent study from I-ELCAP, and perhaps Claudia will talk about it, where they talk about changing the threshold; that's the study shown here on the far right. Please note that the median age in this study was 59, the median pack-years, this red dot, was about 25, and in the NLST the median pack-years was 48, so this data coming from that which extrapolates the number of cancers found and things like that has little relevance to the question at hand.

Here's a pie chart we generated in my office. We just took the list of trusted sites from the Lung Cancer Alliance. We stopped when we got about halfway into the alphabet. These sites publish their screening eligibility criteria. This small blue slice of 19 percent meets the multi-society guidelines for eligibility, the orange meets the USPSTF. Every other site enrolled people who don't meet

those criteria.

Here's an example of a sample we chose, the John Muir Health System. Read the eligibility criteria at the bottom, they'll screen people between 40 and 80 who have a long history of smoking, or people having an immediate family member with lung cancer, or an occupational exposure. That doesn't meet any recommendation.

Every guideline recommends shared decision-making, and I'm asking Medicare to contemplate that in the context of covering CT screening. Why? Risk of lung cancer varies in a predictable fashion and so does the benefit. Decision tools are in development, and this is my fancy slide showing that in fact, every guideline recommends shared decision-making. I'm very proud of that.

(Laughter.)

The risk variation issue, I'm going to show you a paper from the New England Journal, empiric data from the NLST. This is organized in the following fashion: To the left is a hypothetical scenario in which you screen only

the top quintile of patients based on their predictive risk of lung cancer in the NLST.

You'll notice just doing that gets you 38 percent of the lung cancer deaths in the population, and then as you enroll lower and lower risk people within the study, you reach the cumulative number. Bottom right, the ratio of false positives to prevented lung cancer deaths is most favorable, again, focusing on the highest risk patients.

This is a paper that Michael Gould and I had doing the same thing. This is again a modeling study, the top three groups are NLST people, the bottom two are not NLST eligible. Focus only, because there's limitations of time, on the right-hand column. If you go to an individual who fits the typical participant, the number you need to screen, you can tell that person, about 256 people like you need to be screened. The minimum eligible participant was 1,200. Going down to the fourth line, the NCCN recommendation, which you will hear more about today, the minimum eligible person for NCCN, 3,000 people need to be screened in order

to prevent one death from lung cancer, one-tenth as efficacious as the mean in the NLST.

There are some decision tools that are under piloting. Shown here on the left is a handout from the VA which shows two scenarios, to the right not being screened using the NLST estimate of one in 320; to the left, the benefits, the three prevented deaths in the green circle, and the various harms.

There's an active grant from PCORI down at M.D. Anderson to develop video-based decision aids.

And then at the bottom right is a screen shot from our very pedestrian decision aid that's on the Sloan-Kettering website, but which will give you tailored estimates per thousand people.

Here's some thoughts on your questions. Do benefits outweigh harms in the Medicare population? Remember, benefits and harms vary by individual based on risk factors, life expectancy and preferences. What about high risk adults over 74 years of age? There's

no empiric data, there's minimal empiric data over 70. Annual screening beyond three LDCT screens, there's no empiric data, the models I believe are not reliable and they are

fundamentally not in agreement. And outside a clinical study, does it improve health outcomes, again, not meaningful outcome data, and reasons for concerns about selecting settings.

There are good things happening in harm minimization. The American College of Radiology efforts, the BiRADS effort is one thing that is going on. But there's serious concerns in my mind, and I showed you a slide of a place advertising CT screening, that coverage from Medicare will lead to an explosion of inappropriate activities, driven by probably a mix of good intentions and entrepreneurialism. Remember that the coding and capturing of smoking history as an eligibility criterion is something we have no experience with, it doesn't fall under the meaningful use criteria, and we have a long history of behavior by doctors coding things

like minimal bowel symptoms to do colonoscopy screening as our backdrop for this.

How confident are you that clinically significant evidence gaps remain regarding the used of LDCT? And again, large groups of

potentially eligible patients not studied, and they tend to be populations who may derive less benefit and be harmed more, the elderly, the less well educated, et cetera.

Thank you very much for your attention.

(Applause.)

DR. REDBERG: Thanks very much, Dr. Bach, that was very helpful.

And next we have Laurie Fenton Ambrose, who's the president and the CEO of the Lung Cancer Alliance, and you have 15 minutes.

MS. AMBROSE: Good morning. My name is Laurie Fenton Ambrose, and I am president and CEO of Lung Cancer Alliance. I have no personal conflicts to disclose, and Lung Cancer Alliance has received the grants listed.

It is an extraordinary privilege for me to be here today to represent this community

before the panel, and to ensure that the people, the people behind the numbers, and their voices are heard. I can tell you that they know what is at stake. It is a breakthrough they have long advocated for. They know we can transform one of the most

lethal cancers in our society to a curable one with lung cancer screening, and they know there is no reason to further delay or deny them this lifesaving benefit.

It's also an honor for Lung Cancer Alliance to be a part of the largest coalition that has ever assembled on their behalf. Standing shoulder to shoulder are the nation's leading experts in the field that include multiple professional societies, public health organizations, hospital centers, industry, health equity leaders, women's health organizations and patient advocates.

We are carefully -- we have carefully considered this evidence. We have been developing and deploying best practices in the field today, and we are unified and in agreement, and support national coverage for

lung cancer screening for our Medicare population.

With over 160,000 people dying each year, we have lost roughly a half a million people to this disease since the National Lung Screening Trial was halted in 2010. The vast majority of the cases were detected late stage,

and the majority of the cases diagnosed were and will continue to be in people over the age 65.

There is no other proven way to find and detect lung cancer at its early stage when it is most treatable and curable. Expeditious action is not only reasonable, necessary and appropriate, it is warranted. It is a public health imperative for our nation and for our Medicare population. We have sufficient evidence. Lung cancer screening has been more rigorously tested and reviewed prior to implementation than any other screening method, a combined total of over 30 years.

The NLST, as we heard earlier this morning, one of the largest randomized trials ever carried out by the NCI with over 53,000

participants in 33 sites over eight years, with nearly a quarter of a billion federal dollars spent, confirmed the mortality benefit with only three rounds of screening. If time and funding had permitted additional rounds of screening, the mortality benefit would have been even greater.

We have the benefit of the USPSTF

recommendation, which conducted an independent two-year evidence review resulting in a B grade for a population 55 to 80 with a heavy smoking history. That means right now for the non-Medicare population, lung cancer screening is an essential health benefit.

We also have the benefit of the pioneering efforts of the International Early Lung Cancer Action Program, over 20 years of observational research that includes the largest patient registry for CT screening for lung cancer in the world. Its seminal work has led to the development of a well-defined screening protocol that externally validates the conclusion of the NLST and proves responsible screening can be achieved with

minimal harm in a variety of settings, including community hospitals.

The National Comprehensive Cancer Network has been providing updated consensus driven gold standard clinical guidance on lung cancer screening to doctors and patients since the NLST, guiding screening practices at this very moment.

And based on all of this evidence and

clinical work underway, an unprecedented coalition of multi-society, multidisciplinary stakeholders have joined together in a public statement of support for a full and expeditious coverage for this preventive screening service. The threshold of evidence has been met to support Medicare coverage for lung cancer screening within the USPSTF population.

So let's consider three elements, educating the general public about screening and risk, implementing responsible best practices, and supporting quality improvement with the collection of data.

First, it's essential to properly educate the public about lung cancer risks and

ensure that people have the tools and information they need to make an informed decision about whether the screening is right for them, as important as laying out what constitutes responsible care and guiding those people only to places conducting responsible screening.

Lung Cancer Alliance, among others, has developed a risk navigator tool and tailored educational materials that have

already been utilized by thousands of people. We have already launched public awareness campaigns encouraging people to live more moments, targeting this outreach to areas where our screening centers of excellence are located. We're involved in training opportunities, including webinars and CMEs, and we have also been working with higher risk populations, collaborating with the Department of Defense, the VA and veteran service organizations, to inform our military and veteran populations who are at even greater risk than civilians, and to provide them lifesaving care.

In fact, five of the largest DoD treatment facilities, led by the incredible team at Walter Reed, are screening following guiding principles of our national framework of excellence in lung cancer screening and continuum of care, which leads me to the second element, the implementation of best practices.

The full integration of lung cancer screening into clinical practice is well positioned today because of the thoughtful and careful preplanning that began immediately

following the halting of the NLST in 2010. Unlike our other experiences with other screenings, we were and still are ahead of the curve. A multidisciplinary team of doctors, many of whom are in this room today, moved rapidly and thoughtfully to create a blueprint that would launch a community of practice that promotes responsible screening as its norm, and would inoculate against substandard care, and this blueprint is our national framework, it has done just that. The national framework has elevated the national dialogue about responsible screening and created a clinical

culture and mindset around best practices today.

The principles that guide the national framework include informing the patient on risks and benefits of screening, adhering to best published practices, coordinating care with a multidisciplinary team, including smoking cessation counseling, providing prompt reporting to the patient and referring physician, and supporting quality improvements within the process and collecting data.

I am proud to say that this growing

network of centers of excellence has served as a de facto national pilot program. When these slides were submitted a month ago we had 169 centers. Today we have 172 centers in 37 states and in Washington D.C. This network is demonstrating that high quality responsible screening in practice is scaleable, is replicable, and in a variety of settings that go beyond NLST sites. In fact, approximately 70 percent are not associated with academic medical centers, yet they are delivering high quality care, and I want to take this moment to

acknowledge and thank all of the doctors and the nurses, the health care teams, referring physicians including family physicians, who considered the evidence, understood its impact, and moved forward without delay. They are delivering responsible care in the real world in real time for real people. We trust them.

And for those people who currently smoke, screening's added benefit is that it provides a teachable moment to help them quit through more personalized and targeted interventions to achieve success. Like the patients at C.E. Putney Memorial Hospital in

Albany, Georgia, who shared recently that because of their experience with the screening process, were able to quit after more than 30 years of smoking. The cost utility of smoking cessation within screening has been analyzed, and I'm thrilled Bruce Pyenson will speak to this and other issues related to cost in his upcoming presentation.

So now, let's turn to the third element, which is supporting quality improvements with the collection of data. We

support coordinating and building upon existing databases to provide ongoing quality assessment to make continuous improvements to the process, and as screening moves forward we have the benefit of existing registries and data collection, assuring right now the lowest incidence of unnecessary testing or procedures, as well as optimal outcomes of any invasive testing or surgery that is indicated.

An example of how we have already improved and refined the screening process, in February of 2013, the publication of an I-ELCAP paper on nodule size and malignancy based on 15 years of structured reporting and analysis, led

to the revised recommendation to a six-millimeter threshold for a positive scan. Summer of 2013, the recommendation was carefully considered and incorporated in the NCCN clinical guidelines, and the result is that this new threshold will significantly reduce the number of false positives without a significant reduction in efficacy.

To the question regarding the collection of additional evidence, to make

screening for the USPSTF recommendation contingent on the collection of even more evidence cannot be rationally explained or justified. The most important questions that have been raised have been answered. Radiation dosage has been reduced consistent with a level of mammography. As I just referenced, we have made refinements in protocols, adjustments to the threshold nodule size, reducing false positive rates, and screening is already being responsibly implemented within the community and for people over the age of 65.

In fact, nearly half the people being screened in our centers of excellence are Medicare beneficiaries. Coverage with evidence

will not lead to any additional information that will fundamentally change the elements and the practice of responsible lung cancer screening for our seniors, but what it will do, and make no mistake, it will cost time, money, and their lives.

Now, let's talk about what's really at stake, and that's equity and access. The Affordable Care Act makes lung cancer screening

an essential health benefit. The vast majority of private insurers by this time next year will include screening in their coverage. Some already have. If Medicare does not cover screening, we will be faced with the ludicrous situation of a break in coverage at age 65, when risk is greatest. If we limit lung cancer screening only to large academic medical centers or NCI designated cancer centers as contemplated in the request for coverage with evidence, people in areas of high risk will face significant barriers to access.

Let's consider these two maps. This map shows where we have the highest incidence rates of lung cancer in the country. This map shows where the NCI designated cancer centers

are located. If for example we were to restrict screening only to these types of centers, huge swaths of the country would be left out. Even worse, we'd disenfranchise the very community hospitals that are leading the way and saving lives right now --

DR. REDBERG: It's time to wrap up.

MS. AMBROSE: -- beyond the centers

that you'll hear today, Stanford Health in Sioux Falls, South Dakota, Mary Bird Perkins in Baton Rouge, Louisiana, St. Joseph's Center in St. Charles, Missouri, Gibson Cancer Center in Spartanburg, South Carolina --

DR. REDBERG: Time to wrap up.

MS. AMBROSE: Pardon me?

DR. REDBERG: It's time to wrap up.

MS. AMBROSE: Thank you. So in closing, much has happened since the NLST in 2007. We've witnessed advancements in technology, in reductions in radiation and surgical improvements, all contributing to further maximizing this benefit and minimizing the harms. And so to return to the people, in closing, for too long a black cloud of despair and indifference has hovered over this

community. Yet now we have a convergence of solid evidence and best practices that bring tangible hope for their survival. The enormity of the impact cannot be overstated. There is no need to create any additional barriers to this lifesaving benefit that would result in a patchwork system for our Medicare population.

Thank you.

DR. REDBERG: Thank you very much.

(Applause.)

Thank you, and I'd like to now introduce, our next speaker is Dr. Doug Campos-Outcalt, who's the chair of the department of family, community and preventive medicine at the University of Arizona College of Medicine. You have 15 minutes.

DR. CAMPOS-OUTCALT: Thank you. I'm happy to be here today. I was asked to come and explain the position taken by the American Academy of Family Physicians. I am a part-time staff person for the academy, served as a scientific analyst for them. For the past seven years I have been the AAFP liaison to the U.S. Preventive Services Task Force. I have no financial or intellectual conflicts. I would

mention that I do serve on the advisory committee on immunization practices at CDC and also on a group that evaluates genomic test strategies at the CDC. Neither of those have been involved with this issue.

So let me just explain about the

American Academy of Family Physicians. We are one of the largest organizations of primary care physicians other than the internists, and our physicians are located geographically around the country at the same rate as the population of the U.S., so family physicians are distributed around the country, and family physicians see the impact at a local level of recommendations made by national organizations for all types of recommendations, and we're asked to weigh in on a number of different topics.

For preventive services we tend to adopt recommendations that come out of the United States Preventive Services Task Force, and these are for screening, counseling and preventive medications. We rarely disagree with the task force, but we have at times done that. For instance, we think that HIV testing

universally should start at age 18, not 15, and we did disagree with them on lung cancer screening, and our Commission on Health of the Public and Science thought at this point in time the evidence rating should be an I and not

a B, meaning insufficient evidence.

We adopt ACIP recommendations for immunizations and we tend to adopt EGAPP recommendations on genomic prevention issues only, because there has been only one of those so far.

So when our commission looked at the lung cancer screening issue, they had five concerns, and it was the following: First, the recommendation was based largely on one large study, albeit a large randomized control trial of high quality. Our commission felt that the conditions of the National Lung Screening Trial were unlikely to be replicated in community settings. The age of the participants in the trial, you've already heard 75 percent were below the age of 65, in relatively good health. A conservative protocol for working up positive findings, although we've heard actually that there was no protocol, so that's somewhat

reassuring.

And we felt that there would be much less benefit and more harms when this was implemented at a community-wide setting.

The third concern had to do with modeling and extending the number of tests beyond what went on in the NLST, as well as the age range of the population in the NLST.

A fourth concern was that a current smoker who started in at the screening recommendation at age 55, could potentially get 25 annual CT scans, and this gave our members a great deal of concern, and there was unknown harms from accumulated radiation and followup for positive findings after 25 scans. The likelihood of having a false positive is pretty much 100 percent there.

And a fifth concern was there was no cost-benefit analysis.

So we looked at the evidence reports that were published on the website of the U.S. Preventive Services Task Force and as was mentioned before, there were four studies that were looked at, the NLST and then three studies. And the other studies have confidence

intervals that cross the relative risk of one, meaning no significant difference was found. As was mentioned before, these were smaller

studies and of somewhat lower quality.

But the normal thing to do, which the evidence report did, was to perform a meta-analysis and a forest plot, and combine these studies to look at the overall result. And this was an evidence report that was, a separate evidence report which is also on the website of the task force. And if you look at this meta-analysis of lung cancer mortality, it does show that when we do a meta-analysis, they actually eliminated one of the studies here, the low quality one, that the meta-analysis lung cancer mortality does end up in the range of about .8, or about a 20 percent reduction.

If you look at the all-cause mortality, you find the same result in the four studies, three of them don't show any difference, but when you do the meta-analysis here, when you add the three highest quality studies, there is no difference in all-cause mortality, so that has some implications as to potential complications from these

interventions.

So the AAFP Commission on Health of

the Public and Science looked at all of this and considered three different possibilities. One was a B recommendation for three annual tests for those who meet certain criteria, and that we would either determine that exams past three would either be a C, meaning individual discussion and decision-making, or I, meaning insufficient evidence. The second possibility was that we would just say it's a C recommendation for everybody, a C recommendation meaning individual decision-making where the benefits and harms are kind of equally balanced, but there's some people who could benefit, and you get to that through individual discussion.

And the third option we considered was an I statement, meaning insufficient evidence. Our commission chose the insufficient evidence. We felt at this point in time there is just not enough evidence to assess the harms in particular, and we were not confident that the benefits in community settings would equal what was achieved in the NLST.

During the comment period when the

draft recommendations, or after when the draft recommendations were posted, we did make a couple of comments about possibly restricting the recommendation to clinical settings that meet certain criteria, and making a clear protocol for, or suggestions for following up on positive findings. And then we also suggested considering a better risk-benefit patient profiling to minimize the number of CT scans and false positives, and potential harms.

That concludes my statement.

DR. REDBERG: Thanks very much, Dr. Campos-Outcalt.

(Applause.)

Okay. We will now take a break for ten minutes, and we will reconvene promptly at 9:50.

(Recess.)

DR. REDBERG: I would like to reconvene and ask our public speakers to take their seats, everyone has seats over there. So, our first public speaker, and each speaker will have four minutes and I will set the timer, is Dr. Albert A. Rizzo. He's medical

director of the E-ICU, section chief of pulmonary and critical care medicine at Christiana Care Health System, and past chair of the national board of directors of the American Lung Association. Thank you, Dr. Rizzo.

DR. RIZZO: Thank you. I have no conflict of interest to disclose, and as stated, I am a past chair of the national board of directors of the American Lung Association, and speaking here on their behalf.

I want to thank you for letting the American Lung Association share our views on this important topic. We strongly urge CMS to include low-dose CT scanning screening among Medicare's covered services at a minimum for the high risk groups identified by the U.S. Preventive Services Task Force. This coverage would give high risk Medicare patients access to the only secondary prevention method currently available.

The ALA asks the committee to consider some additional points. We urge CMS to be flexible and amenable to changes in coverage consistent when any new findings indicate

appropriate expansion of these screenings in other hybrid populations, such as patients with reduced lung function, chronic obstructive pulmonary disease, patients with certain occupational exposures, and patients with a 30 pack-year history who quit smoking more than 15 years previously.

Both the American Lung Association and the American Cancer Society will be submitting recommendations regarding the additional risks in this population. The American Lung Association requests that CMS put into place methods to ensure rapid progress toward achieving high standards of recommended care in the screening process, and this should include data collection such as patient demographics, smoking histories, comorbidities and imaging technologies, as well as the creation of patient registries, the creation and performance of medical audits, and provision of incentives and accreditation of screening programs.

The Lung Association strongly recommends that CMS require institutions to collect data on all patients undergoing lung

cancer screening, including those that are not currently considered high risk by the USPS task force.

Evidence developed in other populations identified at risk by the National Conference of Cancer Networks such as those with family history, high risk occupational exposures and longer quitting histories more than 15 years will be critical in expanding further coverage for screening and minimizing barriers, so that more appropriate people are screened, and further unnecessary lung cancer deaths are prevented.

The American Lung Association urges the committee to require smoking cessation treatment be offered to any patient screened for lung cancer. Smoking is the most important avoidable risk factor for lung cancer, accounting for approximately 85 percent of all cases. Tobacco avoidance is still the primary way to prevent lung cancer, and lung cancer screening offers an ideal opportunity for an educational moment, and cessation services should be provided to those at highest risk of lung cancer.

Finally, I want to try to put a face, or at least a voice on our recommendations by sharing a personal story from one of our volunteers, Christina. Christina's mother died, would have met the USPS task force definition for being at high risk and worthy of CT screening had the recommendations been in effect even a year ago. This is her statement.

My mother Donna was diagnosed with lung cancer on August 23rd, 2013, and died on October 1st, only five-and-a-half weeks later. I am grateful she did not suffer a long time in pain, but for my dad, my sister and I, there is a hole in our hearts and lives that will never heal.

I know that most people will take up a cause when affected by a preventable personal tragedy in order to try to keep others from experiencing the same thing. I never considered myself a cause type person but I knew that my mom's lung cancer could have been detected so much earlier if she could have been screened with CT scans. Since lung cancer has fewer known symptoms early on, I am convinced

that the low-dose CT scan screening will save

lives by detecting lung cancer much earlier. I urge Medicare to include this screening for high risk patients so that others might have a fighting chance, something my mother didn't have.

So, on behalf of the American Lung Association, on behalf of Christina, on behalf of all the lives that could be saved with lung cancer screening, I thank you for listening.

(Applause.)

DR. SEDRAKYAN: The next speaker is, and I apologize if I don't pronounce it right, Elbert Kuo, from St. Joe's Hospital and Medical Center, and he is the director of the minimally invasive robotic program and surgery.

DR. KUO: I would like to thank the panel for the opportunity to present our two-and-a-half-year lung cancer screening experience, in an area endemic for valley fever and pulmonary nodules. I have no financial relationships to disclose.

Our program was started September of 2011. It's based out of St. Joseph's Hospital

and Medical Center, which is a 500-bed community-based hospital in Phoenix, Arizona.

There are five key aspects to our program.

First, we do a detailed intake questionnaire on all our patients, focusing on their lung cancer and heart disease risks. In addition, we make sure that the patients have established primary care physicians who we can communicate the results to. The patients also have to meet strict hybrid entry criteria to qualify for our program.

Second, we have multiple screening locations throughout the valley that all use the same low-dose CT protocol to minimize radiation exposure. The studies are read by only three dedicated fellowship-trained thoracic radiologists who are involved in our program.

Third, every positive finding is reviewed in a multidisciplinary meeting once a week. Our team consists of pulmonologists, radiologists, oncologists, thoracic surgeons, infectious disease specialists, cardiologists and primary care physicians. At this meeting

each patient is discussed in detail, and individualized recommendations are given based on NCCN guidelines, taking into account the

patient's risk factors and radiological characteristics of the nodules.

Fourth, results along with recommendations are promptly communicated to the patient and their primary care doctor. This communication has been aided by electronic medical records and is very well received by the primary care physicians. The patient is also given a one-on-one physician consultation to go over the results and work on smoking cessation and other lifestyle modifications.

Fifth, we have an active database that all patients are entered in and the data is reviewed regularly.

For those not familiar with valley fever, two-thirds of all valley fever cases in the world occur in the corridor between Phoenix and Tucson. Valley fever is caused by a fungus in the soil, the spores become airborne and are breathed in by people's lungs. This often leads to localized infections and pulmonary

nodules. Because our program is located in an area endemic for valley fever, we expect our pulmonary nodule rates to be higher than other areas of the country. This raises the

question, can the lung cancer screening program be successful in an area with a large number of pulmonary nodules that are not going to be lung cancer.

In our two-and-a-half-year experience we reviewed 512 patients. Of these, 329 have been scanned who met our high risk criteria. As expected, we had a higher pulmonary nodule rate than the National Lung Screening Trial. 50 percent of the scans had a pulmonary nodule, compared to just 27 percent in the NLST. However, we are able to keep our basic testing and imaging rates low with a two percent PET scan rate and a two percent CT data biopsy rate. The NLST rate for the PET scan was 10 percent, and two percent for biopsy.

In our 329 patients we found three lung cancers, a breast cancer, and one patient with lymphoma. In addition, 20 percent of the patients scanned had bad COPD or pulmonary

fibrosis, and 30 percent had moderate to severe coronary complications.

Smoking is a risk factor of both these conditions and their progression. We've conducted a survey of the first hundred

patients one year after their initial screening. 79 percent of the patients either quit smoking or cut down on their smoking. In addition, due to our counseling, 35 percent improved their diet and 33 percent improved their exercise. Counseling after lung cancer screening is a very teachable moment that can result in important lifestyle changes in these patients.

The key to keeping our invasive testing rate down is I look at each patient individually and have information on their risk factors and behaviors based on their intake questionnaire. We take the radiological findings and incorporate them with information based on the patient's intake questionnaire and --

DR. REDBERG: Time to wrap up.

DR. KUO: Great.

And in conclusion, to answer the question, can a lung cancer screening be successful in an area with a large number of pulmonary nodules that are not lung cancer, I think the answer that our program has shown is absolutely. Lung cancer screening can be

conducted in a fiscally responsible manner, minimizing risks, unnecessary testing and patient harm, while saving lives and resulting in important lifestyle changes in a high risk population.

Thank you for the opportunity to speak today.

(Applause.)

DR. REDBERG: Thank you, Dr. Kuo. Our next speaker is Dr. Michael McNitt-Gray, who is the chair of the CT subcommittee, AAPM, and a professor at the David Geffen School of Medicine, UCLA.

DR. MCNITT-GRAY: Thank you. I appreciate the opportunity to come and present to you today. I should also mention that I'm a member, or was a member of a National Lung Screening Trial subcommittee. Here are my

disclosures, institutional and grant support. AAPM has no disclosures, here's some information about the AAPM.

My remarks will be primarily directed towards question two, about the harms of lung cancer screening, which should be minimized from the low-dose CT itself. The target value

that's been stated is 1.5 millisieverts. That's just a little above what the value was for the average whole body effective dose for participants in the National Lung Screening Trial. One of the ways that we helped keep that dose low was develop a protocol chart which I will talk about in a second, and keep specifically the average scanner output which is reported on the scanner, that is the CTDI vol value, less than 2.9 milligray.

The protocol chart was developed in 2002, it was published in 2006. It developed technical settings across 14 different scanners from four major manufacturers at the time, again specifically targeting different technical factors including the CTDI vol which was less than 3.0 milligray for a standard

sized participant with one exception, or one particular scanner. That technique chart was developed in 2002. Again, techniques were low dose, considered low dose at that time. In the intervening dozen years, all scanners have technologies that reduce, allow a significantly reduced dose.

Automatic exposure control methods,

advanced reconstruction methods, advanced detectors, these will also contribute substantially to the dose reduction beyond the 1.5 millisieverts.

That protocol chart developed in 2002 did not require any specialized equipment, these were regular CT scanners, and this can be achieved with the majority of scanners purchased in the last 15 years, so this 1.5 millisievert with no advances in technology is readily achievable and does not require any specialized equipment, but using current technology we can get those values much much lower, significantly lower than 1.5.

So other activities that will help reinforce keeping the doses low during these

scans, the American College of Radiology has developed a practice guideline which will state specifically, make recommendations about technology level and about this dose level, the CTDI vol value, and again, that's a value reported on the scanner itself, so it can be tracked. The designated lung cancer screening programs from the ACR will actually meet these requirements, it will require a minimum CT

technology level and require that the CTDI vol be less than or equal to three milligray, again keeping the dose low for participants.

My professional society, the American Association of Physicists in Medicine, has developed in collaboration with the manufacturers some CT scanner protocols. These have been made publicly available for routine scans such as routine head, routine chest, routine abdomen. This group has made them publicly available outside of its membership and has publicized them quite widely and disseminated them. They are currently working on a low-dose lung cancer screening protocol which, the first version will be made available

next month.

These charts look very detailed, they have a lot of information in them, they are specific to scanners and specific makes and models, but they are targeted towards a specific audience who's going to use these. This is not the lung cancer screening protocol, but it will look just like this but with lower techniques and thinner slice dimensions.

So the 1.5 millisievert effective

dose, I wanted to put that into some context. The average whole body effective dose in the United States from natural sources is three millisieverts, twice that number. Radiation workers such as myself, and radiologists and radiation technologists, are allowed up to 50 millisieverts per year over a 40-year working life.

One of the comments that you should know is that the radiation risks, the actual risk or detriment decreases with age, and decreases substantially, even into the 60s, 70s and 80s.

In conclusion, there is an outstanding

chance of achieving the 1.5 millisievert dose in the participants in any screening program, and there's an excellent to outstanding chance the doses will be substantially lower due to advancing technologies. The vast majority of scanners now can meet these goals, and the ACR and AAPM efforts will help require or reinforce these low-dose techniques. Again, just to put this in context, this low dose, the 1.5 millisieverts is half of what we get, the average person in the United States each

year --

DR. REDBERG: Time to finish.

DR. MCNITT-GRAY: -- and three percent of what radiologists and radiation workers are allowed, and they decrease substantially with age. Thank you.

(Applause.)

DR. REDBERG: Thank you.

DR. SEDRAKYAN: Next is Claudia Henschke, from the Icahn School of Medicine at Mount Sinai, New York. And please disclose any conflicts you have, since we don't have a disclosure form.

DR. HENSCHKE: My name is Claudia Henschke. My disclosures are given here, as well in what I submitted. So, I thank you for the opportunity to talk to you and to answer your questions.

We've had a registry for more than 20 years, and it can be used to address some of your concerns. It started out as two centers in New York City screening 60-year-olds and high risk smokers, and expanded to 12 other sites in New York State with the same risks, and then to 73 sites around the world. We have

jointly screened more than 66,000 participants at this time.

The registry registers all screeners and participating institutions using a common protocol which is regularly updated. It has a web-based infrastructure that provides structured data files or documentation of the imaging, biopsy and treatment findings. The quality assurance program is incorporated in the web-based infrastructure, and this provides formalized training of participating radiologists. We will provide the

infrastructure to the registry for excellence in screening led by the Lung Cancer Alliance and its participating institutions within its framework of excellence and screening, and to the other societies listed here.

We have used this approach, this registry to look at how we can reduce the frequency of positive results and the diagnoses of lung cancers. As shown here, they can be markedly reduced by increasing the threshold and the new threshold has been adopted by others.

We've answered Dr. Bach's comments in

print, saying it's the same for the NLST groups, but we also have a publication in press that looked at the NLST data and shows that the results are the same for the NLST population. On baseline, most of the people go on to the next annual, the first annual repeat screening. Only those who have a nodule of six millimeters and larger will have further workup, and typically that's another low-dose CT scan. The invasive findings are limited to some two percent, and on annual repeat it's the same

thing, most of them are recommended to go to the next annual screening.

So looking at the consequences of that in the U.S. population, looking at those 65 and older leaving the NLST smoking criteria, 13 percent, as shown in red, would have a positive result on the baseline screening, and nine percent on the annual repeat screening, and that would result in 80 percent, again shown in red on the right, to have a Stage I lung cancer diagnosed. Pathology staging is a little lower, 73 percent, and that translates into this 15-year Kaplan-Meier cure rate of 72 percent, so really that Medicare population,

the results are very comparable for that population as for the 55 and older.

We looked at the academic versus community setting and found there were no differences in the frequency of positive findings and the frequency of Stage I, or in the estimated cure rates.

So we think that I-ELCAP, it is the largest ongoing registry, and it provides external validation of the NLST results in a

real world setting in both academic and community practices. This can save lives as long as it is made readily available for those with high risk of lung cancer. Thank you.

(Applause.)

DR. REDBERG: Thank you. Our next speaker is Ella Kazerooni, professor and director of the division of cardiothoracic radiology and vice chair of the department of radiology at the University of Michigan.

DR. KAZEROONI: Thank you very much to the panel for allowing me to present today on behalf of the American College of Radiology. I have no relevant disclosures.

The American College of Radiology

represents more than 36,000 diagnostic radiologists, radiation oncologists, interventional radiologists, nuclear medicine physicians and medical physicists, who are all critical to the quality and safety in dissemination of lung cancer screening practice today. For over three-quarters of a century, the ACR has devoted its resources to making imaging safe, effective, and accessible to

those who need it. The ACR has a long track record of activities in quality and safety, with CT accreditation programs going back into the '80s. Many practice guidelines and standards have been readily adopted and used by radiologists today in practice, an appropriate criteria which guides our use of imaging. We also have extensive experience in registries when needed to answer questions for which there is lacking evidence.

I will leave this on as my last slide, with additional slides providing details to the panel to consider about these activities.

This week at the American College of Radiology's annual meeting, we approved a new practice guideline for the performance and

interpretation of lung cancer screening CT. It addresses who should be screened, when they should be screened, and how they should be screened relative to quality and safety, low radiation exposures, and the frequency of testing.

Importantly, we also released version one of LungRADS. This is based on the 20-year

experience of the ACR with BiRADS, which is now in its sixth edition. Radiologists know how to use and have widely adopted BiRADS in clinical experience. LungRADS is the equivalent for lung cancer screening. If LungRADS is adopted, and we expect our radiology practitioners will take this up widely, they have been calling for it and asking for it from the ACR, it will reduce the false positive rate from the 27 percent seen in NLST to only ten percent. This will substantially reduce downstream diagnostic testing and make lung cancer screening even more cost effective than what has been shown today.

The ACR endorses the USPSTF grade B recommendation for lung cancer screening and believes it's the right thing to do, that there

is definitive evidence that lung cancer screening with low-dose CT can be done safely, with little harm, low radiation exposure, and is the right thing to reduce mortality for this cancer that kills more men and women than any other cancer in the U.S. today.

Under our CT accreditation program we

have also released a new ACR designated lung cancer screening center program designation. This specifically takes into account the training of radiologists to interpret lung cancer screening CT, and the lower radiation CT techniques which are required to do this safely in practice.

We are developing our appropriate criteria modeled after the USPSTF and NCCN recommendations, and are aggressively developing educational programs and campaigns both for radiologists and providers, as well as the public, in patient awareness, to make sure that lung cancer screening is being done in those who need it and it is done well, with attention to safety.

Again, I would like to thank the panel for allowing me to present today on behalf of

the American College of Radiology. Our practitioners are ready, willing and able to perform lung cancer screening CT safely. Many of them, as you've heard already today and will continue to hear, are already doing this in practice, they're doing it safely, they're

doing it using their versions of structured reporting which we are now bringing to bear in a standardized manner for all of them to follow in a consistent manner. And we believe as we move forward with lung cancer screening CT for the patients who need it with safety and quality, and to do the right thing. Thank you very much.

(Applause.)

DR. SEDRAKYAN: Next is Claudia McKee, chair of the -- I'm sorry -- Andrea McKee, I'm sorry, who is the chair of radiation oncology, who will lead a team of people talking for four minutes.

DR. MCKEE: No, I'll explain. Thank you for this opportunity to speak with you today on our experience with CT lung screening. My name is Dr. Andrea McKee, I'm the chair of radiation oncology, but I am here today with

Dr. Carla Lamb, who is of our pulmonary critical care department, as well as Dr. Robert Faust of internal medicine, so that they may speak to any questions that you might have regarding our team-specific roles in our CT

lung screening process, but I will be doing the speaking.

We have no disclosures. Lahey Hospital and Medical Center is a multispecialty group practice and part of the accountable care organization, Lahey Health. CT lung screening is viewed as an integral tool in the management of our high risk population.

In January of 2012 the hospital tasked a multidisciplinary team of physician leaders and administrators to develop a low cost, high efficiency value-based delivery system to offer CT lung screening and its community benefits such that all eligible high risk patients could access the proven lifesaving test regardless of socioeconomic status. To achieve cost productive decentralized screening our program requires the primary care team to partner with radiology to identify, inform and follow all eligible patients.

Overcoming identified obstacles to CT lung screening requires special focus in two important domains, a continuing education campaign run through our cancer services

department, and the development of infrastructure including a structured reporting tool, LungRADS, and database to track findings in radiology.

We follow the NCCN guidelines to define our high risk population. Listed here are the secondary risk factors for NCCN group two. They comprise 25 percent of our patients in clinical practice. Ordering sheets with clear CT lung screening entry criteria are provided to primary care offices to facilitate appropriate referrals into the program. In addition, high candidacy is assessed centrally in radiology through trained CT schedulers and appropriate navigators.

20 to 30 patients enter our program each week; more than 65 percent are referred directly through their primary care physician. The program has screened over 2,100 individual patients and performed more than 3,000 screening exams. The program currently manages

an average of 60 patients per week. A four-page FAQ document is provided to all patients and a physician order is required for

a patient to enter our program.

All scans are interpreted by a trained radiologist but not a thoracic radiologist; our radiologists provide general radiology services at Lahey. Two-thirds of the time there are no actual findings, one-third of patients will have a finding for which an evidence-based recommendation is linked to the structured LungRADS report.

This slide is perhaps the most important one because it demonstrates that through use of structured reporting, we are able to triage patients into risk categories so that only those patients with suspicious findings, those larger lesions or growing nodules, for example, are referred to care escalation, which in our center is defined as pulmonary consultation. The vast majority of patients, 96 percent of them, are co-managed by primary care and radiology, thus reducing the risk for unnecessary testing in those unlikely to have lung cancer. This is an important and

critical feature of the LungRADS system.

Of the small percentage of patients

referred to specialty care, less than half of them undergo an invasive procedure. The rate of intervention and false positives in our program is two percent, comparing favorably to the NLST. We check all policy metrics and benchmarks against NLST benchmarks. Every other month these program statistics are reported to our multidisciplinary steering committee.

Smoking cessation is integrated across the care continuum with the opportunity to engage in teachable moments and help move patients through the various stages of quit readiness.

DR. REDBERG: It's time to wrap up.

DR. MCKEE: Okay. Friendly co-trust and reassurance is essential to a decentralized value-based program. It's important for primary care to trust the system, which they do because they are familiar with BiRADS and therefore very easily adapt to LungRADS, as do the radiologists.

We have data regarding NCCN group 2

specifics which I will skip in the interest of

time. However I will make the point that they were remarkably similar to NCCN group 1, with the only difference being there are more former smokers in group 2 than in group 1, and there is a longer average age of quit in group 2.

I will end by saying that the materials that we have developed in our program are made available to anyone who wants to access them. Over 500 sites across the country have accessed and downloaded our information. In my experience, community centers are highly motivated to understand the important elements necessary to develop best practice programs that will allow them to bring about the unprecedented benefit of CT lung screening to the high risk populations. Thank you.

DR. REDBERG: Thank you, Dr. McKee.

(Applause.)

Our next speaker is Dr. Douglas Wood, professor and chief of the division of cardiothoracic surgery and vice chair of the department of surgery at the University of Washington.

DR. WOOD: Thank you, and my

disclosures are on my title slide. I think most notably, I'm the chair of the NCCN lung cancer screening panel.

And I'm going to completely redirect a portion of my comments in order to correct areas of misunderstanding of lung cancer screening presented by Dr. Campos, and leading to disparate and confusing recommendations from the AAFP that are different than every other guideline on lung cancer screening. Dr. Campos assumed highly protocolized nodule management within the NLST as a reason that the results would not be representative of real world practice. This is a completely incorrect assumption, as noted by several other speakers today. Yet in fact, a disciplined algorithm for nodule management has the opportunity to further lower the unintended harms of downstream diagnostic testing.

Second, Dr. Campos presented the assumption that larger, longer screening duration increases the false positive rate to near 100 percent. However, as presented by Dr. Pinsky and confirmed by all of the radiologists in this room, the opposite is

what's true. Further follow-up scans result in fewer and fewer false positives, not more. It is disturbing that a prominent position of the AAFP is undermined by these incorrect assumptions.

Thoracic surgeons have the expertise to address the potential harms of screenings as they are predominantly related to follow-up testings, biopsies and surgical resection. Surgeons have been very systematic and thoughtful in evaluating how many patients have surgery and their outcomes.

This recently published surgical paper looks at the surgical experience from nearly 32,000 patients from the I-ELCAP lung cancer screening program. 1.6 percent underwent surgery and 89 percent of those had lung cancer, with a remarkable 84 percent 15-year survival, compared to a national rate of a 16 percent five-year survival for lung cancer. Less than two per 1,000 patients had a surgery without having cancer, and nearly all of those were minimal lung resections that would not be expected to have significant adverse long-term consequences.

The well-established method of reducing the harm of screening is the adoption and disciplined adherence to an evidence-based algorithm for patient management. Yet, NCCN guidelines not only make recommendations about the population of patients to be screened, but also provide systematic guidance for virtually every clinical scenario arising from lung cancer screening, and NCCN guidelines have annual updates as new knowledge becomes available. For example, the most recent version increased the size defining an abnormal lung nodule in response to important work published by Dr. Henschke and colleagues, with the goal that this will further reduce testing without an impact on the ability to detect early lung cancers.

NCCN guidelines, developed by a wide breadth of experts in the field, provide guidance that can allow even relatively inexperienced programs safe and evidence-based management algorithms. It can also minimize harms of screening, while achieving the maximum access and availability for lung cancer screening to patients.

NCCN also outlines the risks and benefits of screening, and in this year's update will be adding language supporting shared decision-making between patients and their doctors, so that patients can be provided the best possible information to inform their own choices on whether to engage in lung cancer screening. Thank you.

(Applause.)

DR. SEDRAKYAN: Next is Dr. Charles White, from the Society of Thoracic Radiology, who is the past president of the Society of Thoracic Radiology, and now he's from University of Maryland.

DR. WHITE: Okay. Well, again, I want to thank the panel for allowing me to speak, and as past president of STR, I wanted to tell you that first of all, I have no disclosures, and second, to give you a little bit of a rundown of what the Society of Thoracic Radiology is.

It's a society that's now closing in on 35 years old. It's the largest society of thoracic imagers in the United States and

25 throughout the world, with over 750 members

1 with wide representation in the United States,
2 residing in over 45 states, and also has both
3 wide representation in the academic and in the
4 community setting. The mission of the STR is
5 to promote excellence in cardiothoracic imaging
6 and improve patient care through research and
7 importantly, through education as well.
8 Improving patient care, I'll start
9 with that, we've talked about image quality,
10 and as Dr. McNitt-Gray mentioned earlier, this
11 is also part of our mission, to optimize image
12 quality, decrease radiation dose, and in
13 addition to that, to provide best practice
14 education to radiologists and other
15 practitioners. There's also a commitment to
16 thoracic imaging research, and in particular to
17 lung cancer screening.
18 To give you examples of the Society of
19 Thoracic Radiologists' education and research
20 efforts, there is an annual meeting, of which
21 the largest component is really a review course
22 for the practitioner. There is also a website
23 which is available with cases that they

feature, and multiple downloadable lectures, including educational lectures on lung cancer

screening. And importantly for this panel, cutting edge research, including lung cancer screening with low-dose CT, for which most of the members, most of the involved PIs were members of the STR, including everybody here on the speaker list, to my knowledge is a member of the STR. I-ELCAP as well consists of large numbers of STR members.

Other STR member efforts that are going on include a joint ATR-STR lung cancer screening training course that is being developed right now to be presented at the ACR educational center, and as well, a day-long symposium categorical course that will be presented at the very least at the next STR meeting, so this is an ongoing and intense effort.

We would like to recommend broad national coverage for lung cancer screening with low-dose CT based on the NLST results and the USPSTF recommendations, and also CED for other groups at high risk that do not fall

specifically within the above categories, with patient registry enrollment. Thank you very much.

(Applause.)

DR. REDBERG: Thank you. Thanks, Dr. White, and next we have Dr. Richard Frank, who is the chief medical officer of Siemens Healthcare and chair of the Medical Imaging, I'm guessing, Technology Alliance coverage committee.

MS. ELLIS: Excuse me, I have an announcement. We are not allowed to take pictures or recording, so please stop taking pictures and recording today's meeting. The meeting is being broadcast live via CMS, so if you would like to go back and see the meeting, you can do so. So again, please refrain from taking pictures, or we will have to have your cameras and your phones -- I'm sorry -- we will have to take your cell phone. Thank you.

DR. FRANK: Good morning. My name is Richard Frank, I'm the chief medical officer at Siemens Healthcare, speaking today on behalf of MITA, the Medical Imaging and Technology

Alliance. MITA is the leading trade association representing innovators of medical imaging, radiotherapy and radiopharmaceuticals, and appreciates the opportunity to contribute

in today's deliberations.

MITA and its members develop quality standards for medical imaging equipment, in particular for dose reduction. The reductions in exposure achieved over the last decade of innovation have dramatically improved the risk-benefit ratio in favor of annual cancer screening procedures.

Last year's B recommendation by the USPSTF in favor of coverage for low-dose CT in lung cancer screening has been further validated by ongoing accumulation of clinical evidence of the safety, efficacy and efficiency achievable by implementation of this lifesaving screening procedure in the high risk Medicare population in the community setting. Early detection and accurate diagnosis in lung cancer enabled early and appropriate therapeutic intervention with the prospect of a better outcome for the patient achieved at a lower

cost to the health care system.

The CT community has developed a set of quality standards. Participation in this initiative was broad, including notably the FDA, the American College of Radiology and the

American Association of Physicists in Medicine. MITA member companies have incorporated these standards in their product design to enable quality images at lower doses of radiation. Among these dose standards, the most relevant to today's deliberations is NEMA standard XR-29, also known as MITA smart dose, which includes four components: DICOM structured reporting of radiation dose; pediatric and adult reference protocols for image acquisition; Dose Check, which is a set of alerts and alarms prior to scanning if the dose exceeds preset levels; and automatic exposure controls.

In compliance with those standards, here are seven innovations the industry has implemented in the last few years. Given our time constraints today, I'll highlight only one of them. Automatic exposure control helps

optimize the dose for each patient given the diagnostic task. This feature adjusts the exposure to use only what is needed to achieve the required image quality. This feature is now standard on CT systems.

Innovations in CT detectors and image

processing have maintained image quality while reducing exposure to levels well below ambient radiation. The dose necessary for lung cancer screening is a fraction of the dose for standard chest CT because it is inherently easier to characterize the nodule when it's surrounded by air. For comparison, this slide shows the average dose in the National Lung Screening Trial or NLST, as compared to a typical dose for standard chest CT at the time of that trial. This difference has led to the use of the descriptor low-dose CT. Because ongoing innovation continues to reduce the dose emitted by CT, the phrase low-dose CT over time may refer to progressively lower doses. Indeed, the dose typical in the ongoing I-ELCAP registry already is half that in NLST, and much lower doses are being achieved already at

institutions with the most modern hardware and software.

The clinical benefits of these innovations are gained in practice through the efforts of professional societies. The dose registry maintained by the American College of Radiology has led to less variability in dose

across the participating radiology departments, and an overall reduction in average dose in clinical practice. Consistently low exposure in the community setting will further benefit from the widespread use of the standard acquisition protocol developed by the American Association of Physicists in Medicine.

In summary, the USPSTF's favorable recommendation is substantiated by ongoing accumulation of clinical evidence for safety, efficacy and efficiency being achieved already in community settings. Exposure in low-dose CT already is low, and ongoing reduction in exposure will result from innovations by technology companies, the ACR dose registry, and the AAPM's acquisition protocol, tipping the risk-benefit ratio strongly in favor of

screening for lung cancer on an annual basis. Early detection and accurate diagnosis in lung cancer enabled early and appropriate interventions, with the prospect of a better outcome for the patient achieved at lower cost to the health care system. Thank you.

(Applause.)

DR. SEDRAKYAN: Next is Vickie

Beckler, who is the lung cancer screening coordinator from WellStar Health System.

MS. BECKLER: Thank you, thanks for allowing me to present today. I'm actually a nurse at WellStar, and I'm responsible for the largest community-based screening program in Georgia, and neither WellStar nor I have any financial conflicts of interest today. WellStar is a not-for-profit health care system located in Metro Atlanta. We are accredited as an integrated network cancer program by the Commission on Cancer. We have five hospitals, four health parks in five counties, and serve more than 1.4 million area residents. We have performed more than 3,000 lung cancer screening CTs since 2008 and have more than 1,300

patients in our program. We were early participants in the I-ELCAP lung cancer screening trial and we coauthored the National Framework for Excellence in Lung Cancer Screening and Continuum of Care.

We monitor patient outcomes and track our data, and our biopsy rate is less than three percent, and actually 63 percent of our lung cancers through screening were detected at

an early stage. This is four times the national average of only 15.4 percent.

As followers of this document, all screening is performed through a dedicated program, through a multidisciplinary team of physicians, and despite what was presented earlier from the National Office of Family Physicians, our program was strongly supported and is strongly supported through an engaged partnership with our local family doctors, and nearly one half of all of our patients report they were referred to our screening program as a result of a conversation with their local primary care doctor.

Patients are assessed for eligibility

using NCCN criteria and are required to sign a disclosure acknowledging risks. We screen at ten medical imaging centers, all accredited by the American College of Radiology, and we use specific scanner protocols to ensure lowest possible radiation dose, which is approximately one millisievert. We follow a comprehensive process for image interpretation and management of lung nodules.

Patients may elect to participate in

outcomes research through our registry, which we're very proud of. Screening results are promptly communicated to the patient and the primary care provider by following rigorous protocols as set forth in the framework. We minimize unnecessary costs, time and potential harms associated with screening in isolation.

The power of lung cancer screening is in early detection and saving lives in a cancer that is expensive to treat in the late stage, and one of the most financially burdensome to not only Medicare but the entire health care system. What if 85 percent of those diagnosed were detected early versus late? The financial

savings to Medicare alone from a stage shift in detection would be staggering. Do we really need another complicated systematic review or another expensive research study? The evidence is indisputable, lung cancer screening saves lives.

We embrace some of the concerns that were discussed or voiced earlier today. In fact, we all want the same thing, to ensure that lung cancer screening is conducted safely and responsibly, with rigorous protocols to

improve patient outcomes and reduce mortality.

Every screening procedure has inherent risks. The real life experience of our program, in contrast to the theoretical statistical analysis, demonstrates that the system of multidisciplinary care minimizes risk and maximizes benefit in lung cancer screening, even in a community-based program. These results can be replicated and performed safely in local hospitals and centers which deliver comprehensive patient-centered cancer care across this country on a daily basis. As a matter of fact, more than 170 community

hospitals already do so by following this framework.

The NCI estimates that only 15 percent of cancer patients in the U.S. are diagnosed and treated at the major academic cancer centers. The vast majority of these patients are treated in community hospitals near the communities in which they live. People deserve access to safe affordable lung cancer screening and care close to home.

DR. REDBERG: Thank you.

MS. BECKLER: Please do not impose

unnecessary barriers to access, please support the U.S. Preventive Services Task Force recommendation for lung cancer screening, and thank you for your time and consideration and opportunity to be here today.

(Applause.)

DR. REDBERG: Thank you. Next is Dr. Richard Wender, chief cancer control officer at the American Cancer Society.

DR. WENDER: Thank you, I appreciate the opportunity to be here. I'm here wearing two hats, because I also chair our lung cancer

screening guidelines committee. While chair of the department of family and community medicine at Thomas Jefferson University, I then subsequently became chief cancer control officer at the American Cancer Society, so I'm representing both viewpoints. Other than chairing that guideline, I have no conflicts of any kind.

It's thrilling to be able to say that the major cancer screening guideline groups have achieved a high level of consensus regarding guidelines. ACS, the task force, NCCN all recommend that lung cancer screening

be provided to populations at high risk. You've heard the presentation of AAFP, but for those guideline groups who engage regularly in screening guidelines for cancers, there's a high level of consensus.

There are some differences and I will comment on those briefly. At this time most of the U.S. organizations do endorse the NLST entry criteria for lung cancer screening, I think it's important that the panel understand that this is actually a relatively high bar for

near-term absolute risk, and as has already been mentioned, I do believe we will be able to refine risk criteria over time to identify those who are particularly high risk and perhaps those who are at lower risk.

The USPSTF had one caveat that they actually withdrew eligibility once the individual was beyond 15 years post smoking, smoking cessation, which was not the protocol used in NLST, when you were eligible you remained eligible, and that is what the ACS recommends. We do not comment, ACS, about the use of combination of risk factors, and appreciate the opportunity to continue to look

at risks and eligibility.

Thus, ACS recommends that Medicare beneficiaries should be covered for annual lung cancer studies without co-pays or deductibles if they meet ACS criteria for age and smoking exposure. This recommendation also applies to surveillance exams following a positive finding on CT screening. The ACS has considered the recommendation of the task force to extend the screening age to 80, and can support coverage

for otherwise healthy 80-year-olds who meet established criteria. And as mentioned, if we are going to expand this eligibility, that we would support a coverage with evidence program.

Three final points: This trial, the NLST was conducted with three annual CTs conducted in a two-year period from 2003 to 2005. As you have heard repeatedly, it is very likely, virtually certain that the ratio of benefits to harms has substantially improved since that time, and that additional benefits will actually be seen with annual screening rather than the three screens within a two-year period, zero, one-year and two-year.

Second, a phrase of 18 percent

over-diagnosis was mentioned. That's using an extremely conservative and probably inappropriate way to measure over-diagnosis, which is the ratio found at the end of the screening period. To calculate over-diagnosis these patients need to be followed ten to 15 years, and it is virtually certain that the over-diagnosis rate is far lower than 18 percent.

Finally, we have substantial evidence that's been presented that this program can be implemented with a high level of accuracy and safety in many settings around the nation. The best way to improve quality is to provide this service with accreditation, with the kinds of programs that we've seen, with quality monitoring, with incentive payment, that's the best way to improve quality while making this test available to all eligible individuals. Thank you very much.

(Applause.)

DR. SEDRAKYAN: The final scheduled speaker -- not the final, I'm sorry -- the next speaker is Jody Ruth Steinhardt, who is a coordinator at Maimonides Medical Center.

MS. STEINHARDT: Good morning, and thank you for the opportunity to speak about the importance of Medicare coverage for lung cancer screening. I represent Maimonides Medical Center, a community-based hospital in Brooklyn, New York. We have no disclosures.

Our comprehensive program brings together pulmonologists, radiologists, thoracic

surgeons, nurse practitioners and health educators for a full complement of services. Referrals come for a variety of sources with the overwhelming majority being from physicians.

All patients who come through the program are screened at intake for appropriateness using the National Lung Screening Trial criteria. On the day of the scheduled appointment patients are met at the door, informed of the risks and benefits, escorted through the CT scan, and then contacted via phone and mail with results and followup as dictated by protocol. The primary care physician is an integral part of the team.

Because we recognized that on a population basis, primary prevention is more

effective than secondary prevention, we have also integrated a smoking cessation initiative into our screening program. Screening participants who are current smokers are strongly encouraged to quit, and offered access to our smoking cessation programs. We use the American Lung Association's freedom from

smoking curriculum.

Brooklyn has the highest population of older adults of all five boroughs of New York City. Our residents are ethnically diverse with almost half of them having been born outside the United States. They are economically diverse as well, with many representing working class families, some of whom are living at or below the poverty line. These groups have a high prevalence for smoking or past smoking, and have an increased risk for developing lung cancer.

We are all too aware of the cost in human lives due to lung cancer. Maimonides Medical Center has a Commission on Cancer designated cancer center where tremendous resources, both financial and otherwise, are spent trying to help patients with late stage

disease. Unfortunately, as this committee is aware, despite the best intentions and the most recent treatments, when the disease is diagnosed at a late stage, not only are these treatments often ineffective, but also use a disproportionate number of resources. The cost

of treating late stage lung cancer is astronomical.

I think of a recent patient who happened to be a colleague, who presented with Stage IV lung cancer. Despite aggressive, often debilitating treatment, nine months later she passed away. The cost of her care was in the hundreds of thousands of dollars. The cost of a lung screening and finding malignant disease early is far more cost effective, to say nothing about the decreased physical and emotional toll on patients and their loved ones.

Once the findings of the National Lung Screening Trial were published, showing a 20 percent decrease in lung cancer-specific mortality, we felt compelled to mobilize all of our resources to form a multidisciplinary lung cancer screening program. When our program

started a year ago it was a fee for service model where patients would pay $150 per scan. Since many could not afford this out-of-pocket expense, there was such backlash from the provider community compelling us to find a

funding source. I am happy to report that we were successful and that funding was made available for 200 scans, of which 106 have already been completed. Unfortunately, once these funds are exhausted, we may not have a way to provide the service at low or no cost to those at high risk of developing lung cancer. We've projected the funds will be used in October of this year, just five short months from now.

Since the beginning of this program, several patients have reported back to us that they have stopped smoking because of their experience going through the screening process. We are aware of the theoretical criticism that low-dose CT screening programs may cause unnecessary anxiety and unnecessary procedures. We also know that some say that implementing the rigorous standards outside of the context of a research study might be challenging.

We're here today to enthusiastically say this is not the case. We have set up safeguards and criteria to determine who to screen, how to screen, and how to direct

follow-up results of the --

DR. REDBERG: Time to wrap up.

MS. STEINHARDT: -- low-dose CT scans based on published criteria. We know that there's a great need for lung cancer screening from the number of people who have already come through our doors, and considering the increasing older adult population and increased risk of lung cancer with age, it is imperative that screening for lung cancer become a covered benefit under Medicare. Thank you.

(Applause.)

DR. REDBERG: Thank you. Our next speaker is Dr. Dan Raz, who is from the division of thoracic surgery, and director of the tobacco exposure program, and codirector of the lung cancer and thoracic oncology practice program at the City of Hope.

DR. RAZ: Thank you. These are my disclosures.

I wanted to share with you the

development of our lung cancer screening program at City of Hope where we implemented expanding use of meaningful use criteria to

identify patients eligible for lung cancer screening as well as tobacco cessation.

At our institution we have an integrated lung cancer screening and tobacco cessation program that is led by an advanced practice nurse who's also a licensed tobacco cessation expert. We use NCCN lung cancer screening eligibility criteria, and we do not use an absolute upper age limit, nor do we exclude patients with severe COPD from screening. These are because these are two of the highest risk groups for lung cancer, and safe and effective treatment options exist for these patient populations.

We currently use the NCCN lung nodule management protocol and as we have no primary care affiliation, we've expanded upon the CMS meaningful use tobacco questions and developed what we call the tobacco screen to identify patients who are eligible for lung cancer screening as well as for tobacco cessation. This screen was administered every six months

for ambulatory care patients and recorded directly into the electronic health record, and

was well received by the clinic staff.

In our initial experience, reports were generated and patients were contacted by the program nurse to discuss screening. We're not implementing automated alerts to physicians so they may electronically refer patients who are eligible to the program for consultation.

During the first seven months of implementation we identified 420 patients who were eligible. Unfortunately, 110 patients who were willing to pay the out-of-pocket expense enrolled in our screening program and in addition, more than 40 percent of these patients underwent tobacco cessation counseling.

While the incidence scans had a 32 percent rate of detected nodules, only three patients or 2.6 percent underwent a biopsy. All of these were transthoracic needle biopsies and all three of these patients had Stage I non-small cell lung cancer. In other words, no patient without lung cancer underwent invasive testing, and that remains true still in our

screening experience. All three patients with

screen-detected lung cancer, the first three patients actually were treated with stereotactic body radiation therapy, due to severe COPD and use of home oxygen or other patient factors.

SBRT is a low risk curative treatment option for patients who are a high risk for surgery, and is contracted standard of care for this population with Stage I non-small cell lung cancer smaller than four centimeters. The efficacy of SBRT is well described in Stage I lung cancer with local control rates of approximately 90 percent for cancers smaller than three centimeters.

In conclusion, augmenting meaningful use tobacco questions is a reasonable method of identifying patients eligible for both lung cancer screening as well as tobacco cessation, and it can be implemented by tracking using electronic health records. Automated alerts to primary care physicians would be the most efficient method of implementing this, and in our and other centers' experience, lung cancer screening is safe and it results in very few

diagnostic procedures in patients who do not have a lung cancer when a nodule management protocol is followed. We and others have evolved in our management of nodules based on and since the data that Dr. Bach presented, to minimize invasive procedures.

DR. REDBERG: Time to wrap up.

DR. RAZ: Okay. I just want to make clear that a positive scan does not mean a thoracotomy. We have minimally invasive methods of detecting lung cancer and of treating lung cancer, especially in patients with advanced age, where minimally invasive lobectomies and lung resections can be performed with mortality rates of one to two percent, and sub-lobar resections of less than one percent, and SBRT is associated with very low morbidity and excellent outcomes for patients with limited lung function or otherwise who are at high risk for surgical resection. Thank you.

(Applause.)

DR. REDBERG: Thank you, Dr. Raz.

DR. SEDRAKYAN: Next, we probably have one speaker, or two, sharing four minutes,

Francine Jacobson and Michael Jaklitsch, from American Association of Thoracic Surgery. I mean they're from Brigham and Women's Hospital, but representing the American Association of Thoracic Surgery.

DR. JACOBSON: We stand here together. I am Dr. Francine Jacobson, a thoracic radiologist, here with Dr. Michael Jaklitsch, a thoracic surgeon, in our capacity as cochairs of the Lung Cancer Screening and Surveillance Task Force of the American Association for Thoracic Surgery, to convey our specific recommendations for lung cancer screening. We have no financial disclosures to make. Relative to the National Lung Screening Trial, it is proper for me to disclose that I was the site PI for Brigham and Women's Hospital as a participating site.

Following the NLST, we reopened our program for clinical screening using criteria based on NLST, and have continued to move that criteria in accordance with best recommendations, including the United States Preventive Services Task Force.

We do take exception to what we call

the quit rule, about 15 years, and we remind the panelists that the entry criteria for the NLST specifically excluded those with a previous lung cancer.

DR. JAKLITSCH: The AATS specifically recommends annual screening beyond the limited entry criteria of the NLST trial, to include Americans up to the age of 79 if they have preserved functional status. There are several justifications for screening through age 79. First of all, half of all lung cancer victims are over the age of 74 years. Secondly, America is maturing and is expected to continue to mature, with an average life expectancy of 78.6 years. The risk of developing lung cancer is dependent upon age, and Americans between the ages of 74 and 79 years have a disproportionate benefit from lung cancer screening. This observation was specifically confirmed by mathematical modeling by the USPSTF and published as an addendum to their December 2013 public statement. The USPSTF recommended screening to age 80.

The peak incidence occurs in men over the age of 75 years and between the ages of 71

and 80 years in women. Furthermore, risks in smoking men and women exponentially increases as a function of age. Lung cancer screening must include Americans between the ages of 74 and 80, or the most vulnerable group will be denied the benefit of this detection. Since the elderly population has a higher rate of the disease, we are confident that the NLST trial would have been more significant if they had not been excluded from participation in that trial.

We remind the panel that previous lung cancer victims were specifically excluded from the NLST trial because of the recognition that they have a higher risk of new lung cancer compared to the general population. After five years, they are considered cured of the initial lung cancer. This highest risk vulnerable population of over 400,000 lung cancer survivors, including some never smokers, and in particular female never smokers, needs to be covered by low-dose CT scan screening. We appeal to you -- oh, I'm sorry.

DR. JACOBSON: Don't be sorry. We

appeal to you to drop the quit rule. It has

unintended consequences, illustrated in the following example: Two individuals, perhaps a couple, enter a lung cancer screening program at age 55 and both enroll in a smoking cessation program. One is able to quit but one is not. At age 70 the individual with the successful smoking cessation experience is no longer covered by the quit rule, just as she is about to enter the age associated with greatest risk.

DR. JAKLITSCH: The continued --

DR. REDBERG: It's time to wrap up.

DR. JAKLITSCH: The continued smoker, however, still benefits from screening because he continues to smoke. The general public will see this as unfair and discouraging to smoking cessation.

DR. JACOBSON: We have absorbed into the handout another slide that shows how we use the modeling criteria and things that can be done through risk assessment to move forward, and we would like to thank the panel for the opportunity to present the logic behind the

AATS recommendations. We owe a debt to smokers who have provided the data to demonstrate the

ability of early detection to change the natural history of lung cancer, and look forward to gathering the data to refine the benefit. Thank you very much.

(Applause.)

DR. REDBERG: Thank you. And our next speaker is Bruce Pyenson, who is the principal and consulting actuary at Milliman, Incorporated.

MR. PYENSON: Good morning. I am a fellow of the Society of Actuaries and a member of the American Academy of Actuaries, and for the past 27 years I've been employed by Milliman, a large actuarial consulting firm. I'm here as a private citizen. My employer, Milliman, consults to the majority of insurance companies in the United States and probably the world, as well as companies that have interests, diverse interests, including interests in manufacturing and scans.

I'm one of the few non-clinicians in the room, but I'm following in the footsteps of

actuaries who early on, perhaps a century ago, recognized the connection between tobacco and lung cancer, and also developed the survival

models that are used today to measure survival in cancer.

An actuary's work includes measuring and protecting the solvency of insurance organizations, including Medicare, as well as coming up with costs and financial forecasts. I've published several articles on the costs and consequences of mortality of lung cancer and lung cancer screening, and I'm going to give you some information today from very recent work that was funded by the Early Detection and Treatment Research Foundation, specifically on the Medicare population.

I want to talk about the cost and the cost benefit of screening eligible Medicare enrolled smokers and ex-smokers aged 55 to 79 using low-dose CT scan and follow-up protocols that have been developed by clinicians. The results I'm going to present are based on detailed models that are really deterministic actuarial models that combine life tables,

decision trees, incidence rates, cancer stages, stage shifts, and treatment costs.

On the cost of lung cancer screening for Medicare, my estimate is the cost is one

dollar per member per month, and that assumes about a 50 percent takeup rate of the approximately four million Medicare eligibles who would be, beneficiaries who would be eligible. The total cost would be about $600 million, or approximately one-tenth of one percent of Medicare annual spending. We assumed based on the literature that about nine percent of Medicare beneficiaries would meet criteria for screening, and the one dollar PMPM is based on assuming that about half of them would get involved. That's probably a high estimate, so the one dollar per member per month is probably too high for a number of years.

We assumed that, this is based on an annual screening and followup for five-millimeter diameter nodules, but that would go down if the threshold were increased. Now in our pricing of that one dollar PMPM, we

recognize that there would be no cost sharing for the initial CT scan, but follow-up CTs and follow-up biopsies would have typical beneficiary cost sharing, and these are 2014 dollars and based on 2014 schedules.

DR. REDBERG: Time to wrap up.

MR. PYENSON: The basic other finding is that the dollars per life year saved is in the $20- to $25,000 range, which compares very favorably with other forms of cancer screening.

So just in conclusion, I've looked at a lot of things, this is one of the best valued population interventions I've seen, and I think that CMS actuaries with their data would come to the same conclusion. Thank you.

(Applause.)

DR. SEDRAKYAN: Now I get to correct my mistake, so the final speaker is Dr. James Mulshine, who is a professor of internal medicine and who is associate provost for research and vice president for research at Rush University.

DR. MULSHINE: Yes, thank you very much. It's a privilege to be here for an

incredibly important topic. I have no relevant disclosures.

I have been heavily involved in lung cancer research for the last 30-plus years, 20 of which were at the NCI where I had the privilege of working with a number of people

here, directors of the institute, in launching what became the NLST, and it's incredibly gratifying to hear the evidence that is being shared with you today.

I would just like to highlight a few things. In terms of lung cancer screening, we've already heard from Dr. Pinsky that this is very special, this is the most dominant lethal cancer in our world and in our nation, and it's one of the few opportunities through cancer screening that we have. In fact, it's probably unique in that it will potentially result in an overall all-cause mortality benefit. That is quite remarkable and needs to be thought about very very carefully, because this is a population-based tool that actually can have traction in the war on cancer in a way that has eluded us in the past.

We've heard an incredible amount of information about generalizability, and in fact the key aspect of that is that generalizability information has been delivered with a very very strong focus on discipline in terms of mitigating harms and costs, and wear and tear on the target population. We've heard some

information about concerns about the generalizability, the mortality reduction benefit of this service, and I would ask you to please go back to the U.S. Preventive Services analysis, because they dealt with this in a very comprehensive way. They pointed out, as shown in the table, that the two trials that no mortality benefit was demonstrated was the result of two small trials with essentially 10 percent of the accrual to those trials as to what we saw in NLST, they had a much smaller duration of followup, and they were in low risk populations, so the number of events was quite suspect. Relative independent power calculation said it's really an inappropriate comparison, and they deal with it very politely in that analysis, and I would encourage you to

look at that again.

And similarly, that analysis was very useful in looking at other issues in a much more comprehensive way than we've heard today about issues like quality of life and other things, where they surveyed very comprehensively the existing literature, and they found in fact there was no significant

evidence of harm.

The issue of over-diagnosis, Dr. Wender touched upon it, and it is critical. And the 18 percent number is in fact probably an over estimate, and one of the key reasons for this is that because in that paper that was published on that subject that came up with the 18 percent number, they included the management of bronchioloalveolar carcinoma, which is a very benign acting form of carcinoma which has been subsequently reclassified by the International Association for the Study of Lung Cancer to be part of a noninvasive management, i.e., it's not a disease that is recommended for operation. And if you in fact follow contemporary guidelines as the thoracic surgery

societies in our country do and as the NCCN guidelines reflect, you do not operate on that, and you eliminate the single largest contribution to over-diagnosis in that calculation.

DR. REDBERG: It's time to wrap up.

DR. MULSHINE: The final thing I would just say is that lung cancer at 85 to 90 percent, is a disease of smoking. Smoking is a

habit which tobacco companies have preyed on our youth and have resulted in addiction of a large number of our population. The Surgeon General has spoken about this in great detail, and we unfortunately know that the ravages of smoking are principally visited upon populations that have less economic resources, less educational background, higher educational background, and is particularly vulnerable. And so creating barriers to access to these most critical populations for lung cancer risk is from a public health perspective extremely disconcerting, and I would ask you to think about that very carefully in your deliberations, as I'm sure you will. I will

stop there.

DR. REDBERG: Thank you, Dr. Mulshine.

(Applause.)

I want to thank all of our presenters. We have four nonscheduled speakers who have all signed up, they will have one minute each. Instead of going to the podium, I ask you to speak from the microphone, and please remember to disclose any conflicts of interest or state that you have no conflict before you start.

Thank you. Our first speaker is Andrea Borondy Kitts.

MS. KITTS: Thank you. I'm a retired aerospace engineer and lung cancer advocate. I draw on mutual funds and last week I signed a consulting agreement with Lahey Hospital and Medical Center to provide patient-centered input into their lung cancer research study.

I lost my husband Dan to lung cancer in April last year. Dan had many of the risk factors. At the time of his diagnosis he was 69 years old, an 80 pack-year smoking history, quit 11 years prior, had COPD, and his sister died of lung cancer at age 63. In January of

2011 I talked to Dan's primary care physician about screening for lung cancer using low-dose CAT scan. His physician had not heard about the National Lung Screening Trial results, did not recommend the test, and my husband did not want to pursue it because Medicare did not cover the test. In October of 2011 Dan was diagnosed with Stage IV non-small cell lung cancer and 18 months later, at 10:21 a.m. on April 12, 2013, he died in my arms.

Lung cancer screening was too late for

my husband but it's not too late for those yet to come. Thank you.

(Applause.)

DR. REDBERG: Thank you. Next is Christine Berg.

DR. BERG: Good morning, and thank you. I'm Dr. Christine Berg, I'm currently an adjunct professor of radiation oncology at Johns Hopkins. I was formerly the head of the National Lung Screening Trial at the National Cancer Institute. My conflict of interest is that my husband owns some General Electric stock.

I have two issues that I wish to discuss. One, the mortality benefit from low-dose CT that we reported in our primary outcome paper was 20 percent. We had some dilution with lung cancer emerging after screening ended, so it's as Dr. Pinsky reported this morning, with additional followup it fell to 16 percent, and in my opinion that's a result of dilution.

One sentence in our paper that was presented this morning I would, as the corresponding author, I would like to say that

we probably didn't write it optimally. The divide is not between community and academic centers, the divide is with those centers committed to a total quality improvement approach which is critical, and I think that's where the emphasis should be, professional societies should be developing the guidelines for optimal screening. Thank you.

(Applause.)

DR. REDBERG: Next is Amy Copeland, from the Lung Cancer Alliance.

MS. COPELAND: Good morning. I'm Amy

Copeland, director of medical outreach for the Lung Cancer Alliance, and in that capacity I manage our screening policy and programs. I have no financial disclosures.

I just wanted to share some thoughts from community cancer centers with whom we work, who would be affected by this decision.

From the center we work with in Grand Rapids, Michigan: We are a community hospital with the nearest academic institution hundreds of miles away. We have screened over 300 patients, with six being diagnosed with lung cancer. If screening were limited to academic

institutions, the majority of our population in west Michigan would not receive this lifesaving screening.

From the center in Spartanburg, South Carolina: Of 50 people screened, one was diagnosed with Stage I lung cancer, result was surgery. He was rural and would not have traveled any more than he was already traveling. The closest academic centers are about four hours away. The lower socioeconomic status areas we serve are unable to drive those

distances. Thank you.

(Applause.)

DR. REDBERG: Thank you. Next is Gabriele Geier, and if you are representing an organization, just tell us if the organization has any financial conflicts of interest.

MS. GEIER: Sure. We have no financial conflicts. I am Gabriele Geier and I am from the Lung Cancer Alliance as well.

And just to add to what my colleague Amy just said, from Odessa, Texas. The closest academic medical center is 360 miles away. The majority of our Medicare population does not have the financial resources to travel this

distance for a lung cancer screening. Restricting access to academic clinical centers will cause a severe disparity in our population. Thank you.

(Applause.)

DR. REDBERG: Okay, thank you very much. We have now heard from all our presenters, and we now have an hour for the panel to ask questions to the presenters. I want to invite all of the presenters, well,

we'll get you organized, to come sit up here in the first row, and I would suggest that people just signal me and I will just write the names down. And I think as we do have quite a number of presenters, if there's someone to whom you want to address your question, you should let that be known.

And so I'm going to address my question in particular to, I think Dr. Pinsky, because we're talking obviously a lot about the National Lung Screening Trial, which was clearly a very well done trial, you know, high quality randomized clinical trial. My question has to do with the choice of using chest x-ray in the control, because it clearly, you know,

we know that chest x-ray is not effective in lung cancer screening, the U.S. Preventive Services Task Force looked at that a number of years ago, and my concern is that it's not really in the screening arm, so that you have the same sort of harms from looking at a chest x-ray when you're doing a comparison to CT, there's nodules seen, there's additional testing. A lot of the harms that, we're trying

to balance the advantage of screening versus no screening, but both of the arms really were screening, so we're really just looking at two different kinds of screening and not screening versus no screening, and I'm just curious if you would comment on that.

I note in the paper it says that's because that was being studied in the PLCO trial, but I'm just concerned that we're not really looking at screening versus no screening.

DR. PINSKY: Yeah. When NLST was started in 2002 the results of the PLCO trial, which was comparing chest x-ray versus no screening, were not available yet, so we figured that the two trials combined would give

an answer of low-dose CT essentially versus usual care or no screening. So that's sort of how that came to be, and then when the PLCO results came out just about the same time as the NLST results, and that showed essentially no difference between chest x-ray and usual care screening. So in that sense we figured that the mortality rate in the NLST chest x-ray

arm would be essentially a surrogate for what mortality would have been with no screening, so that's sort of how that came about.

Some of the other trials in Europe, I think, do use an actual no screening arm.

DR. REDBERG: Right, and those trials show no benefit.

DR. PINSKY: Right, and they're very small underpowered studies.

DR. REDBERG: Maybe we'll talk more about harms later on. Dr. Sedrakyan.

DR. SEDRAKYAN: I wanted to start with the probably most crucial evidence here, as to the estimate of the effect. So we have heard about a 20 percent reduction in mortality and we heard also that it moved to 16 percent reduction in mortality as you recalculated the

estimates at the end of the follow-up time period.

So the question is for Dr. Pinsky and Dr. Bach, in fact. Then when you've done some sensitivity analysis, you presented the data on older patients, relatively older, the over 65 group, the estimates look like .87 for the

hazard ratio. And we also heard from Dr. Bach and many people here today that in fact with older age, the higher chance of cancer, and essentially the benefit should be higher. So we're not seeing that in your estimates. Can you comment about this evidence, why is it moving towards one rather than getting stronger estimates of the effect in the over 65 population?

DR. PINSKY: Well, there's two ways of really looking at the benefits. One is the relevant risk as a percentage of mortality reduction, and that was either .80 or .84, and when we did that stratified by age, we did find based on the overall .84 that it was .87 for the 65 plus, but that difference was not close to being statistically significant and the trial was not powered, really, for an

interaction analysis. So even though they, you know, the point estimates were different, we don't really think that's evidence that the percentage, mortality reduction is necessarily different in the older age group.

But besides the percentage reduction,

the other way of looking at a benefit is by number needed to screen, and the number needed to screen takes into account also the underlying mortality of the population, so if they have a similar percent mortality reduction but the older age group has a higher lung cancer mortality rate, the number needed to screen is going to be lower, and the number needed to screen was about 245 in the 65 plus and 360 in the less than 65, so by the measurement of the number needed to screen, it was more effective in the older age group.

One other point is the number needed to screen, again, is the number needed to screen in this case the three-year, three screens, to prevent one cancer death, but it does not take into account life years, number of life years saved, so in that sense this might be a little biased in terms of the older

age group because for each life saved you're saving less years of life than if you save the life of a younger person.

DR. SEDRAKYAN: I think that --

DR. REDBERG: I just want to say for

the reporter, that was Dr. Paul Pinsky, and when people are commenting, please give your name first so the reporter knows who's talking.

DR. BACH: Peter Bach. I basically agree with Paul, I think there is several moving parts here. One is, as Paul noted, that the subgroup analysis by age was sort of unplanned and underpowered, and I don't think there's stark evidence that we did age difference, the relative risk was fairly homogenous.

In terms of the number needed to screen, it's driven by the baseline risk of death from lung cancer largely, and so we would expect as you go into an advanced age to be around the efficacy endpoint.

Paul is right, you have to be a cold hearted economist to look at this this way, but nevertheless, the life expectancy prolongation per each averted death is reduced as people get

older. So in terms of the net benefit, the intersection between the number needed to screen and life expectancy prolongation is one that is tricky and as I showed earlier, there's

this other issue. The 60-day mortality rate following surgery in the NLST was one percent. That's lower than we see in any other observational study, and it was in a young population. In a real world, as age rises, risk rises, and that mitigates the end benefit along the way.

DR. SEDRAKYAN: Thank you.

DR. REDBERG: Dr. Bach, while you're there, and if you could bring up slide 29 from Dr. Peter Bach's presentation, and I'll state because from some of the presenters you might get the impression that lung cancer screening is going to prevent lung cancer deaths, but when I read the data, that's not really what I read. I read that the absolute risk reduction was .33 percent and obviously people still died of lung cancer in the screening group, some people were saved in the non-screening group, you know, and then we're talking about the odds.

So what I wanted to ask is in your decision tool slide, which I think is very helpful for people to actually understand,

because I think everyone thinks yes, if I do get the CT, I won't die from lung cancer, but clearly we heard that 332 people would have to get screened, and one person, one lung cancer death would be prevented, assuming the assumptions of the National Lung Screening Trial.

The decision tool on that slide 29 says that there were three deaths that were prevented in the group that was screened compared to the non-screened group, to the chest x-ray screened group, but that three people developed a major complication from the invasive procedure. So it seems that there was the same number of people getting a major complication from the screening, and of course that was with the, you know, sort of lower incidence of followup and lower mortality, as there was. And I guess that was sort of -- was I reading that slide correctly, because the actual numbers --

DR. BACH: Let me explain the slide to

you. It's not the one that's shown there, but I can describe the slide to you.

DR. REDBERG: It says 29 of 33.

DR. BACH: I don't have the numbers here, unfortunately, but it shows on the left the VA decision tool, it had what Rita's describing, the number of deaths from lung cancer absent screening, and then the sort of suite of events that could occur, this one.

DR. REDBERG: Yeah, that was it, the one with the colors that you just had.

DR. BACH: Yes. So I think Rita is looking at the left-hand side. This is a VA decision tool, it's anchored to the NLST primary results, it's not tailored to the individual, but this is what you're looking at. And if you will, this shows this sort of balancing of the harms and potential benefits of people who are screened. It is always the case with screening that the vast majority of people face a risk of harm, while a very small percentage face the risk of probability of benefit, but the benefits in the case of this averted death and things like that, substantially outweighing the risk to the

individual.

How the calculus worked out as the harms mount and the risk falls, it's a tricky issue, certainly above my pay grade, but the issue on this card that's displayed nicely is that there are harms that are meaningful, and there are prevented deaths. It would be a misrepresentation, of course, to tell people that they will not die of lung cancer if they're screened, but the relative risk reduction of 20 percent seems fairly robust.

This, by the way, is why I think it's important in every single published guideline now, that individualized decision-making driven by the kind of information on this slide, and even better, tailored to the person's individual level of risk, and as I said, our best attempt at doing that is in the lower right, that sort of information really should help individuals decide if screening will have future tradeoffs for them that they find preferable or not.

DR. REDBERG: Thank you. Dr. Hiatt and then Dr. Grant, and just name the slide that you want brought up.

DR. HIATT: Yes, this is for Dr. Henschke, and there was a slide that was not projected. Slide 15 in that presentation showed data from a publication around those who had a much more significant smoking cessation experience, it's slide 15 in your presentation, and it's for those in a CT program, CT screening program. Thank you, that is the correct slide.

And I was curious whether you or others might know whether this in fact was the situation in the NLST, and if so, what contribution does the smoking cessation make towards improved mortality?

DR. HENSCHKE: Thank you for your question, this is Claudia Henschke. This is data from ELCAP, the initial screening cohort of a thousand people 60 and older, and it shows, and it's performed by Dr. David Burns, who was part of the initial report, and it shows that over time going out to five years that people continue to stop smoking, so that screening does not encourage them to smoke, there may be one or two, but overall you see that the smoking goes down.

Now what was the second part?

DR. HIATT: I guess my question, did the same thing occur in the NLST, and was there a difference in smoking cessation between the chest x-ray and the CT group?

DR. HENSCHKE: Okay. I'm not an investigator in the NLST, but this was without even having any smoking cessation program in place, because this was our early studies, before we started putting smoking cessation in.

DR. HIATT: Dr. Pinsky, if you could answer that, I guess where I'm really going, is there a difference?

DR. PINSKY: Well, we did look at smoking cessation in the NLST, and this is data from what we called the LSS, which was about two-thirds of NLST. So if you take at baseline the current smokers and then we ask them every year if they were continuing to smoke. And the quit rate in the CT arm, if you had a positive baseline screening, the quit rate was about 11 percent, meaning that on all subsequent yearly surveys you said you did not smoke currently, and for a negative screen it was about five percent.

So it's pretty low rate quitting, a little higher with a positive screen, and the chest x-ray arm was actually almost identical, so you also had 11 percent quitting with a positive screen and about five percent quitting with a negative screen.

DR. REDBERG: Dr. Grant, and then Dr. Gould, and then Dr. Mock.

DR. GRANT: I just wanted to follow up on the matter of effect size. I looked for it in all the stuff I read but couldn't find it, and I'm not sure who can answer that, but I'll start with Dr. Pinsky. If you were to take an average 70-year-old in the NLST, if lung cancer was detected, how many quality adjusted life years would be added, and what is the uncertainty around that for the individual? And let's just take the entire screen sample, say of 70-year-olds. How many expected quality adjusted life years are added?

MR. PYENSON: This is Bruce Pyenson and the answer is, which I don't have with me, in the publication PLOS of 2013 where we applied quality adjusted life years, so that's the source.

DR. GRANT: Right, I read that, but that didn't address the question of the Medicare, the elderly population, so that addressed the 55 to 64.

MR. PYENSON: Yes, it was 50 to 64.

So the reference, then, and speaking as an actuary to give some approximations, obviously for the Medicare population the future lifetime is lower, and that's why the dollars per life year saved for the Medicare population, the 20 to 25 is higher than for the commercial population, it's not quite twice as high. So because of the increasing incidence of cancer over age, most of the life years saved that we were getting from the 50 to 64 were from the older age of that. And the other characteristic of the Medicare population is that even now the impact of baby boomers is significant, that there's a big bolus of people who are people who are 65, 66, 67, because of the baby boomers, and the population size falls off dramatically, so that not quite doubling is still relevant there.

I believe the science of quality

adjusted life years is perhaps not so precise

as other aspects of the modeling, so I'm not sure we have the ability to really fine tune that for the Medicare population.

DR. JAKLITSCH: Although I don't know of direct evidence that cancer --

DR. REDBERG: State your name, please.

DR. JAKLITSCH: I'm sorry, I'm Mike Jaklitsch, I'm a thoracic surgeon who gave a presentation for AATS.

Although I don't know of direct evidence that provides that, there is several pieces of indirect evidence. Obviously the life table analyses from insurance companies show that everybody is expected to have ten to 15 years in that age range. It's not until you get up to about age 80 that you drop to seven years of like expectancy, specifically in Caucasian males.

What is interesting in the lung cancer screening trial is that the lung cancers that are detected are really early stage cancers, so the overwhelming majority are Stage I. But more than that, they're actually smaller than

other Stage I's. So if you look at the evolution of survival of Stage I lung cancer

that has been reported in different eras, that was generally about 60 percent for Stage I in the 1980s, then that came up to about 70 percent in the 1990s, early 2000s. In these trials it's 88 percent ten-year survival and as Dr. Wood pointed out, 84 percent 15-year survival.

So these are really much earlier stages. Why? Because there's not the occult nodule that's missing with radiographic staging of these patients, so you really are finding earlier cancers and you really are providing higher cure rates for that patient population.

DR. REDBERG: Dr. Pinsky, did you want to address this question?

DR. PINSKY: If you look in the U.S. Preventive Services Task Force recommendations they have a table of life years gained per lung cancer death averted, and for screening starting at age 60 and ending at age 80, it was roughly about ten years. So that would be if your life was saved by screening, then you

would have ten additional years.

DR. REDBERG: That was based on their model?

DR. PINSKY: That was based on their modeling group that ran the data to age 80. That's why they did the modeling.

DR. REDBERG: Just clarifying, that's from modeling, not actual data. Okay, Dr. Hiatt. I'm sorry. Dr. Gould.

DR. GOULD: Yeah, another question for Dr. Pinsky. You gave us interesting and reassuring results about heterogeneity of treatment effects by age but if I'm not mistaken, there was another paper that came out recently looking at it by sex, and there was a suggestion that screening might be less effective in men than in women, and I'm wondering if you could share those results with us.

And then my second question would be, tell us a little bit more about the implications of downstream outcomes of patients who had incidental findings outside a nodule or a cancer in the NLST, whether on balance the

incidental findings resulted in more harm than help, or the other way around.

DR. PINSKY: The first question, we originally published a paper about the NLST

results stratified by age and also gender, as well as some other categories, and we found a borderline significant interaction in that the effect was, the mortality benefit was actually greater in women than men, as you say. The relevant estimate was .73 in women and .92 in men, and that was with a P value of interaction of .08.

Now when we looked in more detail at the distribution and everything, I won't go into detail, but there was some indications that maybe it was just a chance finding in terms of men having more small cells, that might have been just a chance finding that made it seem like there was less benefit, so that is still an ongoing area of research, I would say. So there is a possibility that maybe there's a difference there.

And the second question was about non-lung findings. Yeah, I think it's sort of

analogous to the situation with CT colonography where we don't really know, you know, we see these other things that aren't related to the cancer being screened for, and it could be a double-edged sword in terms of maybe there's

some benefit in catching these things early, maybe there's some harm in doing the additional workup, maybe there's extra costs involved. So, I think the actions and comments of the NLST is doing a more rigorous analysis so they can collect specific data on the non-lung findings followup. I don't know if anyone else has comments on that.

DR. REDBERG: Dr. Pinsky, another question on the -- so, you told us 96 percent of the nodules were not actually cancers that we're seeing, but a lot of those patients, it seems to me as I read your trial, were told to wait some variable amount of time, three months, six months, a year for repeat imaging. What were they told at the time about their findings, and did they spend that year essentially thinking they might have lung cancer?

DR. PINSKY: Well, we had a standard positive screening letter that said, you know, you have a positive screen, and I think there was language saying this doesn't mean you definitively have lung cancer but it's something, you know, that you should work up.

And then usually patients in a three- or four-month period would get a diagnostic CT or some other followup. I mean, we are doing some quality of life, you know, measures to see, measure the anxiety associated with having a positive screen, and I think there are some short-term anxiety and maybe quality of life deficits, but that is fairly short term.

DR. REDBERG: (Inaudible).

DR. PINSKY: I think there were some studies in which it was more than a half, and in one it was one-third, but they did some more detailed studies, including quality of life, and that may be ready for publication, I'm not sure if they've reported that yet.

DR. REDBERG: It looks like Dr. Jacobson wants to comment.

DR. JACOBSON: Part of what you're

looking at has to do with the harmonization, but within the Akron portion of the trial the initial, when we started, the followup was to be three months, and the first patient we had who actually had lung cancer, by the time she came back at three months, we had changed the followup to six months. So the inconsistency

is not entirely random from what practice is, although in clinical practice it's not uncommon sometimes to see a recommendation that would be three to six months, so you can think of it in that kind of way.

But as a PI, I had the actual contact with the patient and at the time, because you're going back to 2002, we had just started learning about what these early lung cancers looked like, so it was a very honest thing of not knowing for sure what we were looking at. We are much quicker to jump on early lung cancer now than we were then, and it was also for our patients who participated in NLST more comforting and less concerning.

The patient I'm describing actually got referred for some pulmonary rehab, and when

she came back in six months she told me that she had regained her ability to climb stairs and sit on the floor and play with her grandchildren, which she retained after she had the definitive surgery for her lung cancer.

DR. REDBERG: I thought you were going to comment on the quality of life data.

DR. JACOBSON: The quality of life

data was collected in NLST, it was a very extensive set of questionnaires, and patients were contacted in the Akron side on an every-six-month basis to get both their medical experience that was outside the trial, and also to assess with standard questionnaires their quality of life and activities of daily living.

DR. REDBERG: And is that reported somewhere? I haven't seen it.

DR. JACOBSON: I think it will come out. It's probably not immediately available in print yet.

DR. REDBERG: The trial was completed five years ago.

DR. JACOBSON: The number of writing groups in that trial are quite large. I'm

probably not the best person to speak to the stage of the writing groups because I have moved over and become involved with COPD screening, and we have an enormous number of writing groups, and 50 years from now all of these activities will come together to improve the health and decrease the deaths from lung cancer and the morbidity from other tobacco associated diseases.

DR. REDBERG: Thank you.

DR. MULSHINE: Jim Mulshine. The Linda Humphries article from the U.S. Preventive Services Task Force dealt with the issue of quality of life, cited seven publications, the best of which is from the NELSON trial, which is a large European randomized trial which is still ongoing, but the preliminary results have been published and the diagnostic workup has been published, and their quality of life highlights have been published. And they in fact have very favorable results, very similar comparable distribution of stage, in fact better than the NLST.

They found operative complications and morbidity from the workups that they published on, and it's quite modest in their expectation. The quality of life tools that they used showed no significant adverse quality of life impact, they had some trends that they discussed, but overall it was well received, and that trial in fact will be published in a relatively short period of time, within two years, but it tracks very closely with the results we have been

talking about today.

DR. REDBERG: So, we're going to move on, and the next one is Dr. Curtis Mock.

DR. MOCK: I have actually four questions, but I will just take them one or two at a time. I would like to start first with the whole issue of access. I heard access mentioned a couple of times today but I'm a bit confused. As I looked at a map earlier in the presentation it seemed to be there are certain areas of the country where there's a marked density of these screening centers.

Could you just help me understand, if we use for example the number of centers in

Georgia versus the number of centers in Mississippi, and we look at, the incidence actually is higher in Mississippi than Georgia if I looked at the map correctly. So please help me understand as we look at this globally for Medicare beneficiaries across the country, how do we justify making this available for a beneficiary regardless of where they live?

MS. AMBROSE: Laurie Fenton Ambrose, with Lung Cancer Alliance, and thank you. Access of course is one of the key

considerations, but it's also how we build public health infrastructure at this moment in time to meet that demand and need, and what we have been attempting to do is work from the get-go with community centers, hospital centers around the country who are saying we need to do this, help us figure it out, what type of standards should we be following, and trying to ensure we are doing everything we can to support capacity wherever it could be.

These states, Georgia particularly, has shown extraordinary forward thinking. They have been evaluating this years ago and trying

to build the infrastructure to help meet the demand. Mississippi will get there, and in fact I believe we have a center of excellence that will soon come on line, but it does take time and it is a process within these centers to gather their respective teams, get the buy-in, understand the process, build their infrastructure and then roll it out. But that's what we've been trying to do, is work with them as quickly and responsibly as possible, and go proactively to these areas where there is high incidence across the

country and see where we could start this now, not wait, but start it now.

DR. MOCK: What other criteria can you share with us besides interest at the local site?

MS. AMBROSE: Well, the framework is in essence a blueprint. We have been working on 18 elements that we hope to have as a part of every screening center of excellence. So we did research on where comprehensive cancer centers are located, where are NCCN-related centers, what were the NLST sites, the Akron

site, and began proactively to reach out and build from the get-go a mindset, a culture of consciousness around what really is responsible screening, and how can we move this forward as rapidly as possible, and to also work in collaboration with the community cancer associations, associations for community cancer centers, and all of the state entities, to say this is here, it's a proven benefit, how can we move as uniformly and as responsibly forward now, let's get together, let's figure this out and get to work, and then use you as a mentor for other community centers, other hospitals,

to share lessons learned, and to continue to push this out in that kind of a responsible way.

DR. MOCK: Thank you.

DR. REDBERG: Dr. David Howard.

DR. HOWARD: My question refers or pertains to the screening of the over age 75 population. Studies for colonoscopy showed there was a large benefit for the first screening, but the benefit declines rapidly with each successive screen. If and when lung

cancer screening diffuses into widespread practice, might people who are arriving at age 75, having been screened for lung cancer approximately 20 times previously, all with negative results? So my question is, for people who reach that point, who are age 75 or 76, having had a long history of negative lung cancer screens, are the benefits and harms of lung cancer screening that we observed in the trials, would they grow more or less favorable for that type of population?

DR. BACH: Peter Bach. We don't have empiric data, and that's been pointed out, we can speculate about directionality and it could

go either way. There's basic questions like the frequency, whether or not there's risk in screening more frequently or less frequently. One of the intriguing things, and if you want to read the tea leaves in the data in the NLST, I showed the graph from the AHRQ technical report, and when I noted that black line, the relative risk of death from lung cancer actually went almost immediately to 1.2. We have the primary data now and you can see that

at six months, and that might suggest that a lot of this speculation that long-term kind of pocketed up benefits are not as important, perhaps, as near-term benefits. In other words, lung cancer screening may be more like a vaccine that only works the year you give it, than it does something delayed, a vaccine for example that holds for ten years.

I don't want to over-read the data, I am speculating somewhat wildly, but that's what the data is telling us right now.

DR. HENSCHKE: Claudia Henschke. We've been screening people for a long period of time. Each annual round, different from that first round, provides about the same

frequency of new cancers, and as the age increases there will be more cancers, so it's different from colonoscopy in that sense. So each round and each year provides an additional benefit as a person in this population ages, there are more cancers being detected with the additional benefit that was shown in the analysis.

DR. REDBERG: Dr. Hiatt.

DR. HIATT: This question is for Dr. Frank. I don't know if you have data on this, but I am curious whether the proportion of existing installed CT scanners that actually meet the most current low-dose capability is a known piece of data, and are they relatively evenly distributed geographically, the optimal equipment? I'm thinking that with the economic downturn and deferred capital investment that we may not really have very evenly spaced access to the best equipment.

DR. FRANK: I might invite Dr. McNitt to answer this question as well. Certainly the adoption of more modern equipment is not universal and homogenous, it tends to be in academic centers and then ultimately in

community centers, but the fact of the matter is that the data that I showed you from the I-ELCAP trial already documents half the level of exposure per scan than was in the NLST study, and those do include a significant proportion of community hospitals.

I think there is a small proportion of hospitals in the outlying districts that

perhaps have what might be considered outdated CTs, and so there is a significant role for ACR to interpose registries to capture this information. The dose registry has resulted in a narrowing in the variation across sites in the dose administered and an overall reduction, so I think expansion of that dose registry for all those hospitals will help to get a more quantitative answer to your question, but I think it's a small issue that will resolve quite naturally over the next year or two.

DR. HIATT: So let me ask it a little bit more clearly then. There are a certain number of CT scanners in the country. What percent currently have the dose reduction software and capability of achieving the lowest dose that the newest scanners have?

DR. FRANK: I don't have a specific number, I think the majority of them, certainly the large majority of them do have that software and capability for the doses that you see here. Whether it's 70 percent or 80 percent or 90 percent, I can't say, but my group could take action to provide that

information if it became crucial to CMS deliberations.

DR. REDBERG: Along that line, some of your comments noted that there's evidence that low-dose techniques are not routinely used for lung cancer screening, and that at the same institution a patient one day might get a dose of 1.5 millisieverts, and another day at the same institution get 15 millisieverts for lung cancer screening. And in a survey of radiologists, 834 radiologists published by Eisenberg said half of them did not know the current settings used for diagnostic and followup chest CT examinations at their facilities. Usually the NLST used radiologists that were trained and accredited, but it doesn't seem that is a standard we can now rely on across the country.

DR. FRANK: NLST of course was conducted, I won't say ancient history, but a few years ago, and we've grown from there both in terms of the technology, dissemination of that technology, and for example the protocols to which AAPM referred. So with the advent of

coverage, there will be quality standards and so on that will be disseminated and dramatically enhanced. The likelihood that everyone was using the AAPM recommended protocol, everyone participating in the ACR dose regimen will be informed, so you can be assured that people are not being unnecessarily overdosed.

DR. REDBERG: So you're saying that new quality standards would be, need to be developed.

DR. FRANK: They are developed. You heard from Dr. McNitt what the AAPM are doing, they have protocols already, they have refined those, they are in place. Ella Kazerooni said there are standards, that accreditation and training apply, so those are in place and being rolled out, yes.

DR. REDBERG: Dr. McNitt-Gray.

DR. MCNITT-GRAY: Mike McNitt-Gray. I would suggest that outside the NLST, there is no, there has not been consensus on what is a screening exam, so the response that you would get from radiologists, I think is all over the

place. I think it reflects more of a lack of clear understanding of what the screening program is than it does the doses. I think that in the context of the NLST, I think the activities of the ACR and the AAPM will also help narrow the range and we won't see 15 millisieverts for chest screenings, we may see 1.5 --

DR. REDBERG: How do you know you won't see them.

DR. MCNITT-GRAY: 1.5 millisieverts and below. We're most likely to see the vast majority of the scans well below 1.5 millisieverts.

DR. REDBERG: Briefly.

DR. KAZEROONI: Ella Kazerooni. The ACR accredits more CT scans in the United States than any other organization. We accredit over 3,000 facilities with CT scanners. We have developed an ACR-approved

guideline for radiation exposure for low-dose CT scans. These are practical parameters that we expect radiologists to follow and we are embedding them in our CT accreditation program.

So we do expect these are easily accessible to CT scanners across the country.

As a secondary note, as a thoracic radiologist at our institution, University of Michigan, we load a large number of outside exams into our practice, over 10,000 exams from outside facilities are loaded into our system and we reinterpret many CT scans that come from a diversity of practices. Very few of those are done with anything but doable scans today, and this reflects practices from across the country.

DR. REDBERG: Thank you. I did understand that the guidelines are in place, my concern was whether that was not always the ideal. But I do want to move on, and Dr. Melkus is next, then Dr. Hiatt and Dr. Grant, Dr. Sedrakyan.

DR. MELKUS: This question may be for Dr. Pinsky or Dr. Bach, regarding the questions raised about the evidence based on gender and

age differences and the implications for such. Can you comment on ethnic minority groups?

DR. PINSKY: I think the percent of

ethnic minorities was fairly low in NLST, but it was largely representative of the eligible populations in the U.S., but you know, the groups were five or 10 percent of the total. So it's very hard to make any, unless somebody was way different, it would be very hard to make any conclusions about whether it was different in those populations. But again, that's a good thing to be looking at if we go with a registry or followup of practice.

DR. BACH: Peter Bach, thanks for the question. It's difficult to extrapolate to any group in this case, at least in the context of African-Americans versus Caucasians, which is a comparison study and I was lucky enough to work in that area, there's little evidence that there are underlying biologic or genetic differences that would affect whether or not CT screening works or not, but that is certainly less well studied.

DR. REDBERG: Dr. Steven Woolf and then Dr. Sedrakyan.

DR. WOOLF: Thank you. I have a whole bunch of questions but in the interest of time

I will just limit it to two on the issue of harms, since we talked a lot about benefits.

I'm a little puzzled, and I'm not sure who to direct the question to, there's been a thread in the comments that have been made dismissing or minimizing the significance of the inaccuracy of this test. It's positive predictive value, depending on what numbers we look at, is five percent or lower in the NLST, and may be a little higher, and that's terribly low for a cancer screening test. It means that, you know, 95 percent of the people who have an abnormal result don't have cancer. So although we do see the 20 percent reduction in mortality benefit, if I read the NLST data correctly, out of the 26,000 people who were screened over the three years, 83 deaths were averted, that's the 20 percent reduction, but that means 26,000 minus 83 went through the screening experience and didn't have their deaths averted. So, we have a responsibility to think about potential harms there.

The two comments were made that I want

to understand better is, number one, I think it

was Dr. Wood who said that the assertion from the American Academy of Family Physicians that a long-term screening program over time would lead to increasing proportions of the population having received a false positive result that's incorrect. That seems to go against the basic principles of epidemiology, and I think that's a misunderstanding, I think the point Dr. Wood was trying to make was that over time the positive predictive value improves.

That may be true, but it's also true, as the American Academy of Family Physicians said, as is true for most cancer screening programs that over time the screened population will eventually have a larger and larger percentage of the population that receives a false positive result.

The other question for Dr. Wender was the claim that, the assertions about the rate of diagnosis were overstated. I sense here that the term over-diagnosis is being used in slightly different ways. The technical use that I think Dr. Wender was referring to is the

over-diagnosis of lung cancers that ultimately posed no clinical significance to the patient, but it's certainly also used more generally in the medical community to refer to the diagnosis of conditions other than lung cancer, incidental findings for example, that pose no clinical threat to the patient. But my reading of the data is actually we don't know what the over-diagnosis rate is for either of those things, and I'm wondering whether the intellectually honest answer is to say that's unknown rather than to say it's small or not.

So two questions, why Dr. Wood was challenging what seemed like a pretty basic assertion essentially, isn't it true we don't really know what the over-diagnosis means?

DR. WOOD: So, this is Dr. Wood, since you directed that directly to me, and my challenge to Dr. Campos is a misunderstanding of what's determined as false positive, because over time as shown by Dr. Pinsky in his presentation, a second scan that shows stability shows that the earlier positive becomes a negative, so over time actually the false positives decrease rather than increase

in lung cancer screening, and that seems to be misunderstood by others, and yourself. And I recognize the incongruity of that, but the point is that the accuracy increases over time because of the comparative studies.

And there were other questions about harms which, there were questions about the mortality being in comparison to one percent versus four percent, but all of the current studies, including the SPS national database, have a surgical mortality for lung cancer resections of around one percent now, so it's not four percent, as otherwise quoted.

DR. WOOLF: It's a basic principle of Bayes' theorem if you take a screening scan and repeat it on yourself multiple times, you will increasingly get more false positive results. This is a test with roughly 75 percent specificity. If you keep repeating it, for statistical reasons you will increasingly produce false positive results.

DR. WENDER: Rich Wender. Let me quickly, although I'll mainly address the over-diagnosis, quickly address the question of the false positives. I think it's very careful

in all cancer screening that you look at how false positive are resolved. A false positive that is resolved with additional screening is different than one or two initial images, for example, it's very different impact on a patient than a false positive that leads to a biopsy that did not show cancer, and we saw a lot of data that we're now able to keep that rate very low. I don't mean to minimize that it's not a false positive, it still is, but it's not cancer.

The second thing is the technical points in the trial. The definition of, if you were positive at the first screen you were continued to be a false positive even if it was just the same nodule that was reported. I'm not sure that every site did that, but most sites will continue to call that a false positive after three screens even though it was only that one nodule that, you know, the first screen showed. That's just a more technical point.

Let me comment on the over-diagnosis. First off, just commenting about over-diagnosis of lung, the lung cancer, it was not commenting

about incidental findings, and I agree. The true rate of over-diagnosis for lung cancer as a result of screening is unknown.

I think the critical point was made earlier. We are now seeing through screening a stage of lung cancer that frankly was not previously known or seen in large numbers. We are averting --

DR. SEDRAKYAN: Can we limit our comments to 30 seconds, so we can manage to hear from everyone?

DR. WENDER: My apologies, I tried to do two questions. The death rates that we're averting are much further down the road than we're used to seeing in lung cancer, substituting very long followups to truly measure over-diagnosis between the screened and unscreened group.

DR. BACH: Peter Bach, in under 30 seconds. I think you're both right in not saying anything about incremental false positives for certain. Each time you screen a person, the chance that they will have at least a detected nodule rises. As a proportional

matter, the data suggests that that falls over

time with sequential screening.

On the over-diagnosis issue, there's a couple of moving parts that Paul and I agree on this one, it's probably about 20 percent in the NLST of incremental lung cancers over in the CT versus chest x-ray, and then with the additional followup or catchup, that ratio persists. And remember, chest x-ray itself causes over-diagnosis, it's pretty clear from the Mayo data and the Czech data, and that's all mapped, so if you compare usual care to CT, the over-diagnosis rate would be greater.

DR. RAZ: I'm Dan Raz. One piece of information about over-diagnosis, so we know about this in terms of natural history of untreated Stage I lung cancer from the (inaudible) cancer registry that patients who have diagnosed Stage I lung cancer have about a six percent five-year survival. And granted, that is a population-based study, it's not a screening study; however, the vast majority of Stage I lung cancers are still detected incidentally, so they are fairly comparable to

this screening regimen.

DR. REDBERG: Dr. Paul Doria-Rose.

DR. DORIA-ROSE: This question is for Dr. Pinsky. So, we talked a little bit about subgroup analyses that were done within the NLST, and I wanted to really bring up actually this paper that Dr. Bach talked about that looked at kind of the benefit according to what your risk was, and there was a heterogeneity of risks within the high risk smoking population that was included in the NLST, and one of the things that was reported in that paper was that those with a higher number of comorbidities didn't benefit, and I was just wondering if you had some comment, I know you've done work as well about the kind of healthy volunteer effect in trials, as to how the trial participants would compare to the general population with respect to other comorbidities which may impact the benefit of screening.

DR. PINSKY: In that paper they elected to bring out the lung cancer risks and showed, you know, a differential number needed to screen based on the quintiles of lung cancer

risk. I'm not aware of that part of their paper that looked at comorbidities.

I mean, in general I would say NLST,

especially for that rate of patient history, you know, was healthier and had fewer comorbidities than the overall NLST eligible population in the U.S. I'm not sure how to quantify that, but I think that would be readily accepted data, certainly in terms of COPD and history of MI and other things, so yeah, how that would play out, I don't know.

DR. REDBERG: Dr. Grant, then Dr. Hiatt, then Dr. Gould.

DR. GRANT: That was my question.

DR. REDBERG: Okay, thank you. We'll go to Dr. Hiatt.

DR. HIATT: Thank you. This is for Dr. Bach and Dr. Kazerooni. I was concerned about the variability in the radiologists' interpretations, the rates of the detection, and this was in a relatively controlled environment with training and standards set, and so as you think about it and the American College of Radiology thinks about how to reduce

that variability among radiologists, what can we expect as this rolls out?

DR. BACH: This is Peter Bach. I think you're talking about Paul's slides which

showed the across-radiologist variability, and I don't know where Ella is, but I think she would be better to address that.

DR. KAZEROONI: This is Ella Kazerooni. I think as Paul showed, there was radiologist variability, we saw this dynamic in NLST about detection rates and false positives. We also have to recognize that NLST was performed across a broad geography. We have not delved into the details of other influences of local practice, which could be individuals, it could be geography, if you live in the histoplasmosis belt, if you live in the Arizona area, you would expect to have a larger number of non-cancer nodules at the baseline, but after two years you would call that negative screens.

So it's not clear whether the radiologist variability was necessarily one of skill, because they were all trained, versus

one of the underlying populations that were being screened and the geographic differences of those individuals.

DR. REDBERG: Dr. Michael Gould.

DR. GOULD: Yes. I have a comment and

then a question for the presenters. The comment is to kind of clarify the record. So, there was a suggestion made before that based on data from NELSON, that participants who underwent the screening tolerated it well, had no objection. It's important to note there have been at least two studies of, qualitative studies of patient distress in patients who have been diagnosed with lung nodules. Both were in VA settings, neither were in concert with the screening, but both showed that there's considerable distress in as many as 25 to 50 percent of people who are found to have a lung nodule, and that distress can linger for as long as two years, depending on how long followup continues until lung cancer is ruled out. One of those papers was by Renda Wiener from Boston University and the other one is from Chris Latour at Oregon Health Sciences.

And then my question for Ms. Ambrose, first of all, thank you for your presentation and thank you for the work that your organization is doing, and I think we need to have a frank discussion about generalizability, and to me there's a very very clear tension

here. On the one hand we want to make sure that the technology is available to as many people as possible who can benefit from it, on the other hand we want to make sure that it's done safely, and I think your organization recognizes that.

Given what we know about the highly variable quality of health care in diverse settings throughout the United States, would it not be unreasonable, and would your organization support a coverage determination that says we need to be sure this is done right and these are the following conditions that we would attach to make sure that screening was done safely in the right patients who have the right information, can make an informed decision, get followed up appropriately, and are not exposed to unnecessary harms from false

positives?

MS. AMBROSE: Laurie Fenton, and thank you so much for that question, because clearly it is a goal that every one of us here shares, and that's how do we take a proven benefit and make sure that it is deployed safely and responsibly.

What we were hearing from our patients and consumers is am I at risk, should I be screened, and where do I go, and that's what we attempted to address immediately. And the key is whether or not we need to make screening contingent on the collection of more evidence for the USPSTF population, and I believe that we can uniformly say here, with some exceptions, that we can move this forward, and that we do have structured reporting systems, we have protocols, we have technological capacity, and we have the desire by health care teams to do this, and the key is saying here are the requirements to do this well and right, or the principles, and allow these community centers within the context of those principles to then deploy it based on what their community

needs are. So that's what the guiding principles are saying, and we're seeing it pushed out across the country, but I don't think we have to make screening the population contingent on the collection of more data.

DR. GOULD: How can we be sure that those principles are going to be followed and with no disrespect intended, is it really up to

the Lung Cancer Alliance to determine who is a center of excellence, and would you support CMS having some criteria for who becomes a center of excellence?

MS. AMBROSE: I think we could probably all gather and figure that out, as ATR, STS, our organization among other has done, and that would be a wonderful opportunity to really go through this in far more detail than perhaps time allows here, to then reinforce what is in place, what is being observed, and how we can work together collectively to imbed it properly in public health infrastructure. But I would like to say, please have confidence in the professional societies whose direct responsibility is to set

up these screening criteria and protocols, to know they're doing it well.

DR. REDBERG: Okay. We're going to move on to Dr. Sedrakyan.

DR. SEDRAKYAN: We're going to stop these questions and answers. Because of the purpose of the time, we have a few more questions, and we're close to the lunch hour.

DR. REDBERG: And there are several

more questions.

DR. KAZEROONI: I just want to reinforce the point that was said earlier, the ACR accredits the majority of outpatient CT scanners that are --

DR. REDBERG: You did make that point, thank you.

DR. KAZEROONI: And those criteria are part of that, and CMS recognizes that already today.

DR. SEDRAKYAN: Thank you. I really wanted to go back to the presented evidence about the strength of the data and particularly the lung cancer mortality, all-cause mortality issues that were brought up from the beginning,

and why do we suddenly push the all-cause mortality situation to the back further? Is there any reason we wouldn't consider all-cause mortality? Can someone present the data that would mean that patients value more from dying of other causes than cancer? Is there anybody who would like to comment?

DR. PINSKY: You know, in this context of a cancer treatment trial, all-cause mortality is the standard endpoint, but in a

screening trial the standard endpoint is cause-specific mortality just because the numbers don't make sense when you look at all-cause mortality because most cancers can be a very small percent of all-cause mortality, so the standard in screening trials is cause-specific mortality.

The NLST, I think, is the only cancer screening trial that I know of that has shown a significant overall mortality rate, and that's because of the very high risk population, and lung cancer is high risk.

DR. SEDRAKYAN: My point is, I mean, do we have to speak to the mainstream

interpretation in this situation? Also, as you presented the data on strength of the evidence, the overall data from around the world was certainly moving the strength towards the lung. I mean, we're getting weaker evidence if we were to look at the entire, all of the causes for many of these trials. So my point is, the level of confidence, is that in any way influencing you? Peter, do you want to talk about -- in 2008 you had a publication saying with screening we're not necessarily getting

those cancers that can be prevented. Did you change your opinion based on this large trial?

DR. BACH: Peter Bach. Yes, I changed my opinion. The NLST clearly showed a reduction in advanced stage disease among these screened individuals. It was the highest quality trial. We have these other RCTs but from all of these reports, all these slide decks, they are weak evidence at best, they're underpowered, and because of their duration there was probably some contamination as well, but they were the data.

So the issue, just to cut these things

with the right razor, the NLST showed a reduction in death from lung cancer, showed a reduction in death from all-cause mortality. Because so many patients were at a risk of dying from lung cancer, when we subtract out the lung cancer deaths, there was no longer a reduction in causes of death from other causes that was statistically significant. But the important finding here is that it was not attendant harm from screening causing the deaths from other causes. Instead of a patient for example dying of lung cancer, they die of a

biopsy for the lung cancer, they die of a heart attack because they're worked up for the lung cancer, so that was the issue.

DR. REDBERG: But I would, as a clinician seeing patients, if I were involved in shared decision-making, I think my decision would focus on lung cancer mortality, but I think it's fair to say that the patients care if they're going to live longer, they don't care, you know, what are they going to die of, and so you would have to say, you know, looking at all the data we saw, the all-cause was right

on the one line, you would say you're going to have tests, you're going to have screening and we're going to be worried about lung cancer for some indeterminate period of time, but when you're going to die is not determined.

DR. BACH: Yeah, I don't think I agree with that interpretation of the data, there's a sample size issue that's really important. So I think if we read this and extrapolate to the population as a whole, we would not expect a reduction or even an equal life expectancy, we would expect a small prolongation.

SPEAKER: So you can't see the

all-cause mortalities as one?

DR. BACH: Yes, of course, but they, you know, I think the data from the NLST says that, which is that the all-cause mortality would either be reduced or be shaded towards the reduction.

DR. REDBERG: Okay. We should move on. Dr. Fendrick.

DR. FENDRICK: I have a concern that I want to share mostly with my panelists, but since I've been accused in the past of not

sharing my concerns with the presenters, I will present them now.

So, I spent my career basically trying to implement very targeted clinically nuanced benefits. And I'll tell you that you need to think about something much more simple than CT screening for lung cancer. Colon cancer screening, you don't do it before 50 unless there's a family history, 50 to 75 is okay, 75 to 85 not so, 85, not very good, harmful. We're still spending a billion dollars from CMS screening 85-year-olds, and this raises my concern about the fact that this is a very nuanced population that we're talking about

covering.

If you look at the U.S. Preventive Services Task Force for instance, to get a, under the task force a screening for diabetes, you'd have to have hypertension, which we don't do very well. To screen for abdominal aortic aneurysms, you have to smoke, which we don't even know how to do, and about every commercial health plan I've worked with has no idea how to either provide free AAA screening for smokers,

or give it to everyone, or no one who's smoking, or they're still confused.

So I don't want to talk about venue, I don't want to talk about the data. What I want to talk about here is these are very strict, very strict nuanced recommendations, of which a lot of people are arguing even in those populations whether there's any benefit. I want to hear if anyone, or we'll talk about this later, how confident are we that we will be able to implement a coverage decision around these clinical parameters that we know, at least in any history, we've never been able to do this before. I don't want this to be lung volume reduction surgery. I don't want it to

be lab coli. I do not want this to be PSA.

And I would like to see anyone tell me that they have said that none of these people that are older or sick or have all these other sources that come flying in, that we're now going to spend millions or billions of dollars, and that will harm people. I have reservations.

DR. REDBERG: Okay. Well, now we get

to go to lunch.

DR. GRANT: Mark Grant, I just have one thing. I wouldn't be so quick to discount, I think there are seven European trials underway on, that I think have included close to 30,000 patients. To dismiss them, I think, from the perspective of synthesizing evidence, we clearly have, the NLST is the gargantuan piece there and is an unbiased trial from the internal validity discussion, but I think it behooves us to acknowledge those results and also to anticipate that further results will be coming in rather soon.

Patients were recruited differently in many of those trials, they've talked about other aspects that are important, for example,

some of the psychosocial questionnaires that were included, and so I'm a little bit uncomfortable saying well, we're just going to look at the NLST and make the entire decision or evidence assessment based on that.

DR. MULSHINE: This is Jim Mulshine, I was involved in the NELSON and the Lagos trials. The NELSON is clearly the best of that

breed, the NELSON has been published already in the form of a diagnostic workup in the New England Journal, first author, van Klaveren was the first author. The diagnostic sensitivity of that analysis is three-quarters, 95 percent; the diagnostic specificity was reported as 99 percent, the outcomes were excellent, stage diffusion was very favorable. I agree with you, I think it's going to be very supportive.

DR. REDBERG: Okay. Thank you. We are now at 12:19, so we're a little bit late, so we will come back from lunch at 1:15, so we have essentially an hour for lunch.

(Recess.)

DR. REDBERG: I would like to welcome everyone back, I hope you all enjoyed a

heart-healthy lunch in the CMS cafeteria, and I don't think anyone took a walk today. So we will resume, and on the schedule is discussion among the MedCAC panel, but most of the presenters have kindly agreed to stay, because I think a few of the members have indicated they might have questions, so we will do that

for a sort of brief period of time, because we are at a hard stop, and we obviously have to get our discussions and questions. And I also understand that you wanted to make some comments, so please do take some time now.

MS. BECKLER: Thank you. I'm Vicki Beckler and I wanted to address Dr. Mock's question earlier, or comment regarding Georgia having so many lung cancer screening centers that follow the Lung Cancer Alliance framework. And basically, the state of Georgia by their comprehensive cancer control plan, that was recently rewritten as part of the CDC's national efforts to rewrite the state's plan, took it on as a developmental goal, lung cancer screening, in collaboration with a lot of other organizations throughout the state. So I'm happy to report the state has actually exceeded

what our developmental goal was set at for Georgia.

DR. MOCK: Was that a backbone of the CON?

MS. BECKLER: Pardon me?

DR. MOCK: Was that with a certificate

of need model?

MS. BECKLER: No, it was just part of the developmental goals that were incorporated in the state's plans, the comprehensive cancer control plan state's revision to take on lung cancer screening.

DR. MOCK: Thank you for that clarification.

DR. REDBERG: Thank you. Dr. White I think did not get a chance to ask any questions before lunch.

MR. WHITE: I had a question for Dr. Kazerooni and Dr. McNitt-Gray, and it has to do with the, we've established the existence, I think, of standards. I want to ask about the ACR accreditation process for low-dose CT screening, two questions. One, are the standards for the accreditation process on both the clinical and the physics side

comparable to what was proposed or what was done in the NLST, or are they higher or lower or different in some way? And then I have a second question.

DR. KAZEROONI: Okay. I'm happy to

report that Dr. McNitt-Gray assisted us on the CT accreditation program to help develop the ACR lung cancer screening standards and parameters, so we could both speak to that question.

The ACR is one of three designated organizations under MIPPA to accredit ambulatory care facilities for purposes of Medicare coverage and reimbursement, so currently the ACR accredits the majority of outpatient CT scanners in the United States. Under the CT accreditation program we have developed a specific center of excellence or programs, designated lung cancer screening programs which have lower radiation exposure CT scans, which meet if not exceed in the lower direction the lower limits of radiation exposure that was set by NLST, so we expect through our accreditation program that radiation exposures will be lower than what was

seen in NLST.

MR. WHITE: So, my question is not just about the radiation exposure but about things like the criteria for entering the

screening program, things like that.

DR. KAZEROONI: Yes. So as well, we have standards about the physicians who interpret the lung cancer screening CTs, we have standards about entry criteria and eligibility for lung cancer screening, and we also mandate lung cancer smoking cessation as part of lung cancer screening programs.

MR. WHITE: And the second part of my question would be, if a facility wishes to be ACR accredited for CT and they do low-dose CT lung screening, do you require that they have your credential in low-dose CT screening in order to be accredited by the ACR, or can they be accredited by the ACR in CT, do the low-dose screenings but not feature low-dose CT?

DR. KAZEROONI: So, in order to get the designation of being a lung cancer screening designated center, they have to meet our criteria. These are subject both to adaptation as well as to practice audits. They

cannot receive the designation from the ACR unless they're part of the ACR CT accreditation program.

MR. WHITE: My question's not about the designation, it's a MIPPA-related question. If someone wishes to use the ACR accreditation to qualify for MIPPA payment from CMS, and they wish to do low-dose CT screening, do they need to meet your low-dose requirement, or do you pull the accreditation entirely if they don't meet the low-dose requirements but claim to do low-dose CTs.

DR. KAZEROONI: So, the CT accreditation is a broad one, it does not just cover lung cancer screening CT, it covers neuro CT, musculoskeletal CT, cardiac CT, so the global designation for CT accreditation depends on the type of exams that you perform at your center. Sites can specify the types of exams they perform; for example, some sites don't perform pediatric CT and they would not submit that for accreditation. So if they want to pursue lung cancer screening CT designation, they have to submit and conform to the requirements of lung cancer CT designation.

MR. WHITE: I hate to belabor this but this is an important point. If under your

program someone wishes to do, say neuro CT, they can't just say we're going to skip the neuro part but we're going to get accredited for abdomen, and then continue to do neuro, you don't allow them to do that.

DR. KAZEROONI: If they want --

MR. WHITE: Do you allow them to do the low-dose CT screening if they're otherwise accredited but don't meet your low-dose requirements?

DR. KAZEROONI: So, I think we're kind of saying the same thing but choosing different language. If you want to have designation for accreditation under the ACR lung cancer screening program, as a designated center for lung cancer screening you would be required to follow the requirements for low-dose CT, smoking cessation, and the appropriate population being screened. If you did not meet those requirements, you could not have ACR designation as a center for lung cancer screening.

MR. WHITE: But you could still bill

CMS for the low-dose procedures.

DR. KAZEROONI: As a global question under MIPPA, that's probably already existed. We're trying to improve that by having a specific lung cancer screening designation.

DR. REDBERG: I have a follow-up question to that, and then Dr. Burke and Dr. Rich have questions.

So, my question is sort of from the patient point of view. It's not clear if a patient knows that they're going to an accredited place or not, and then beyond that, as I read from the public comments and from the published literature, even if you have a low-dose protocol, it doesn't mean what a patient gets is actually a low-dose CT. We know, for example, from a published study in the Archives of Internal Medicine, from even patients at the same institution, there was 30, 40, 50-fold variability in the amount of radiation. I know there were hearings held after that study was published and there were some positive changes. Have there been any changes since then that have minimized that variability?

DR. KAZEROONI: Part of practice audit under the ACR CT accreditation program is radiation exposure as a quality standard, so that is an important quality component to this accreditation.

DR. REDBERG: And do patients know how much radiation they're getting from a CT screening?

DR. KAZEROONI: The amount of radiation exposure and how it's implemented varies widely across the U.S. in terms of how information is communicated to patients. As you're probably aware, in some states like California there's a requirement for documentation in the radiology report. What information that is and whether it's the right or the best way to communicate exposure and risk, I don't think people yet understand the answer to that question. Radiation risk is a relative one and they simply report a number without a risk assessment of what that means. Whether it's a two-year-old, a 15-year-old or a 65-year-old, it's very important. To just simply convey a number to a patient without explanation, I think would be inappropriate.

DR. REDBERG: Dr. Burke.

DR. BURKE: So, this is a question for Dr. Pinsky. Dr. Pinsky was kind enough to allow me to look at the paper that he referred to earlier about the results stratified by demographics, including gender, and on Table 2 there's a relative risk of radiation-specific mortality of .87, and a relative risk of death of .82, and these were covariant analyses for the P values, but the .87 was for the over 65 and the .82 was for the under 65, so you can look at stratification by under 65 and over 65 in terms of the benefit.

And just from my conversations informally, I was told that this .87 wasn't a significant value; is that correct?

DR. PINSKY: I mean, it probably would not be just because that's a small subgroup, and the trial was powered to find a significant effect of screening for the whole population. So once you do a stratified analysis, it's unlikely that any given strata is going to be significant.

DR. BURKE: Right.

DR. PINSKY: On the other point, the

.87 versus .82, you know, there's going to be some chance variation and there was no hint of a statistically significant interaction, meaning a statistically significant differential effect by age, even though, you know, they were nominally different from .87 to .82.

DR. BURKE: So, would it be reasonable for me to conclude that the NLST did not find any significant effect in patients over 65?

DR. PINSKY: I think that would be a misleading way of characterizing it.

DR. BURKE: Well, I'm just, I'm looking at the numbers, and --

DR. PINSKY: Well, the way I would characterize it is overall we found a significant effect, and we did not find any evidence of a differential by age. So by that I would conclude that there's evidence that it's effective for all the age groups in NLST.

DR. BURKE: Just to hone in, so the .87 wasn't significant?

DR. PINSKY: Well, I don't recall, but because the over age 65 was only 25 percent --

DR. BURKE: Right, I understand that

it involved a small group and everything else, but I'm just looking at --

DR. PINSKY: It probably was not significant.

DR. BURKE: Okay. So the evidence isn't there for over 65.

DR. PINSKY: I wouldn't characterize it that way.

DR. REDBERG: Dr. Mock, did you have a followup on that?

DR. MOCK: Just kind of an extension of that, if you will. Curtis Mock. The 25 percent that's Medicare age that wasn't supported by that data, if we have 96 percent of that study that's false positive, and 25 percent doesn't represent the Medicare data, my question is really to any of you presenters. Tell me where your discussions are around formulating a more accurate stratification system or an identification system to marry those numbers that are going to get subsequent followup and secondary study.

I want to -- it seems as though there are a lot of clinicians here in the presenters

today. I'm really anxious to know in your

discussions around this topic, where are you going with the comorbidity of the smoker who is aged 66 through 80 now getting a false positive result and subsequent workup? In my experience as a practicing clinician, the patient that's 45 that smokes has significant risks. The patient that's 67 to 76 has additional risks that are quite material. So where in the stratification and the identification of that narrow band that's going to benefit from screening is your discussion?

SPEAKER: So, there have been numerous discussions at the professional society level about trying to come up with a registry system to capture exactly this data. In the STS database, and Doug's probably in a better position to speak about it, he was the former president of the STS, we have ten to 15 years of experience of getting data from the surgeons honed down to specific surgical issues, and it's very easy to build upon that the sort of surgical components that people came to surgery through the screening program.

What we're trying to do is use that as a template to go further upstream and try to

adjust databases like that used in the I-ELCAP study as well, to try to prospectively collect that data, because we really view a revision of the recommendations about every seven years, so they will be revisited and tailored down. There's a lot of new technology that's going to come on line in the next seven years that will probably supersede trying to come up with 30 pack-years and age defined at 80 that will make it a more pure populational risk that you would apply the screening to.

DR. MOCK: So, that net seems to be wide for the next seven years, and that's really where I'm looking to close.

DR. REDBERG: Please make your remarks brief.

DR. WOOD: This is Doug Wood. I think it's a thoughtful question and as noted in many of these presentations, there's an effort by us in our professional organizations to work on creating algorithmic approaches to management that can help decrease variability in how these

workups take place to minimize the unintended consequences of further workup, NCCN being one of those, and that's updated annually. So one

of the things I showed is that, for example, we changed the definition of a positive scan from four millimeters to six millimeters due to new data from the I-ELCAP, with the goal that that makes it yet a step better.

And so we're not perfect, we're far from perfect, but I think we do have aspects of algorithmic approach that can make it better, as capable as possible.

DR. MOCK: Thank you. And then we really do think that these changes we make, even though we haven't done studies to prove it, of course we think that's going to help.

DR. KAZEROONI: I will be very brief.

DR. SEDRAKYAN: Exactly for this topic, ten seconds.

DR. KAZEROONI: Exactly. Ten seconds? LungRADS is a structured reporting management scheme that builds on the data that was from ELCAP and NLST and other studies to make sure we manage patients appropriately. Only one in

ten people getting lung cancer screening using LungRADS will be defined as a positive screen. Most of this is because nodule classification sizes have gone up because we know that is what

we can follow and --

DR. REDBERG: Thank you.

DR. KAZEROONI: -- we know that's based on data that's been collected, so only one in ten will have a positive screen.

DR. REDBERG: Thank you. We're going to move on now.

MR. PYENSON: Bruce Pyenson. Narrowly on the topic of how wide the net is, the net of adverse people in the Medicare population is actually rather narrow based on the NLST criteria, and if you compare that to the screening of mammograms or colorectal cancer screening, cervical cancer screening, it's a rather narrow population that generates the vast majority of cancers. So compared to everything else that Medicare is funding, you already have a much narrower effect, but of course it can get much better.

DR. REDBERG: Okay, thank you.

DR. MOCK: My concern was the variability in followup, that really was the point of my question. How many are we catching and then how many are following up, and is it three months, is it six months, is it three to

six months, so we're looking for standardization.

DR. REDBERG: We have a limited amount of time left and I just want to, if you want to repeat things that have already been said in your presentation, we really did listen to your presentations and read the slides, so if you have new information, but --

SPEAKER: I think the rest of what Ella might have said was that not only are the new thresholds going to reduce the number of false positives, it's a misconception to believe that all those false positives go to biopsy and pathology, and most of them are weeded out with just a little more look, like a follow-up CT, and so when we talk about false positives we shouldn't think of them all as undergoing risky procedures and expensive downstream procedures.

DR. REDBERG: Thank you. Next is Dr. Rich, then Dr. Grant, then Dr. Hiatt.

DR. RICH: Sure, this will be quick. This is for LCA or anyone else who might take it up. Looking at the trials and the three-year, three annual scans, and then

extrapolated to get an annual scan, let's pretend that we decide, or CMS decides that they can't go to the annual scans. What is the minimum amount of scanning that you would see acceptable, clinically acceptable? Is it that they get three annual scans and then get forgotten, or do you repeat that after a three-year rest period, any ideas?

SPEAKER: The risk of lung cancer after tobacco smoking continues, so biologically it made no sense to screen to three and stop, with the data we have at hand right now, and as you heard from Dr. Pinsky, it was not the intention of the NLST to do that.

DR. HENSCHKE: If you wait for three years you're bound to get baseline results, it's as if you've never been screened. The annual is the same, what you find on annual is

the same year after year after year. As the age increases, you find more cancers, but not less.

SPEAKER: The last point that I would make which has not been made before is that the USPSTF did model that, looked at annual scans, tri-annual scans and biannual scans, and their

data is available as well.

DR. RICH: This is for Dr. Wood. Can you describe the surgical mortality? There's been some questions raised that if we really do a lobectomy there is the one percent mortality, but is there an effect of mortality based on a patient's age?

DR. SEDRAKYAN: And to add to that also, please talk about the radio-thoracic surgery and how much it improved the outcomes.

DR. WOOD: Certainly. Doug Wood. So to the first question, 80 is the old 60. We actually take care of 80-year-olds all of the time now in surgical staging populations, and it turns out that because we're good at patient selection, the mortality is not meaningfully different than in younger patient populations.

This is because of selection bias, we certainly as surgeons are good at selecting the best 80-year-olds, but that's what we're supposed to do.

The mortality rate for 80-year-olds is in the one to two percent range, with multiple studies, just as it is for the under 80-year-olds. In terms of vas surgery,

minimally invasive surgery is now widely utilized for both diagnostic and therapeutic purposes. Some of these nodules ultimately have a diagnostic wide resection done by vas which is minimally invasive, with most patients discharged the day after surgery, but the vas is also used therapeutically for low back pain procedures, again with shorter hospitalizations and decreased complications.

DR. SEDRAKYAN: And mortality too, or only the hospitalizations?

DR. WOOD: Actually, not a significant difference in mortality, but a significant difference in complications and hospitalizations.

DR. SEDRAKYAN: Thank you.

DR. BACH: In the SEER Medicare data, which is the reference standard, there's 30-day mortality of 4.5 percent at age 79 to 80. The nationwide inpatient samples with no staging information or good detail on surgical information, but even with the surgical codes, the mortality is about four percent in the general population.

SPEAKER: I just have a quick comment.

As a surgeon there's other mortalities out there, like SPRT that you might find in an 80-year-old that would be a good surgical candidate as a result of screening for lung cancer, and those are developing every day.

DR. REDBERG: Thank you. Dr. Grant.

DR. GRANT: Just very briefly, Dr. Pinsky, correct me if I'm wrong. I just want to go back to the specific stratification by age, that in fact there was none of that in the NLST, and you know, this analysis is relative to -- well, I suppose it's dichotomized, so you really can't prove it, so just to make that clear, the relative effect --

DR. PINSKY: On the question of under

and over 65, there is no evidence of effect by age.

DR. GRANT: Okay.

DR. REDBERG: Dr. Hiatt.

DR. HIATT: So for Dr. Kazerooni, I note, and this may be unique to the prepaid environment without significant cost share, but if our clinicians aren't extremely specific in how they order the chest CT, the patient does not get the low-dose protocol, and perhaps in

the world where the patients have significant cost share and they know that that's supposed to be free, it would be different, but I'm concerned that a significant portion of the studies may end up not being low dose, they may be performed as a regular chest CT, which is more exposure and potential risk, and especially as patients move site to site, they may not know that the patient is getting annual lung low-dose CTs. So how would you defend, protect the patients from that?

DR. KAZEROONI: I would say that there's no difference in CT screening and diagnosis than an analogy with breast cancer.

In breast cancer we have screening mammography, which is a certain number of views, and we have diagnostic mammography, which is tailored for patients who have symptoms or have palpable masses noted.

Chest CT is no different. If you order a screening chest CT for lung cancer, that by definition is a low-dose protocol. If you order a chest CT and you say hemoptysis, that's now a diagnostic clinical CT seeking a piece of information that's outside the

screening setting. So it's concomitant on us to make sure that we're getting the appropriate intake so that we can then perform the right exam.

DR. HIATT: So, would you require for anything that doesn't say screening, that they must indicate the reason for the study? Because that's not all that easy to impose.

DR. KAZEROONI: Currently in order to be reimbursed by a third-party payer you have to have a clinical reason for the examination, so I'm not sure that it's possible --

DR. HIATT: So that, you just answered

it, because we don't send bills to anybody.

DR. KAZEROONI: Oh. To get reimbursed for CT purposes we are required to provide information about what the clinical indication is, and we're required to make sure that they're appropriate.

DR. REDBERG: Thank you. Dr. Gould.

DR. GOULD: Yeah, a question for Dr. Bach. We've heard several speakers talk today about the advisability of starting registries to monitor the outcomes and the safety of screening in other settings, and I

know you've written about this. Can you give us an idea of where they should sit, who should be responsible for them? Are there a lot of moving parts, as you say, and you know, it's encouraging that thoracic surgeons have a registry, but that's two percent or less of the patients who undergo screening. So, do these run out of radiology departments, do they run out of some centralized statewide agency, what are the options, what are the pros and cons?

DR. BACH: Peter Bach, thanks for the question. There's not a single answer to this.

In the Medicare system you will see a number of different platforms for gathering data, a registry can reside in a variety of different places, in a professional society for example for the implantable cardiac defibrillator registry, which had separate reimbursement like was done in the PET registry which was done in collaboration with a couple professional societies as well. I think it's unlikely that it would be contained within the Agency, I think that's unattractive, and one of the things I think we're hearing here today, if I can reinterpret it, is that there is actually

quite a bit of interest in doing some quality improvement, and the registries become a backbone at least of that.

There's an issue that although they're indirect evidence of efficacy or harm, just the simple counting of false positives for procedures that are done or that just show how often lung cancer is detected are basic elements, I think. Under CED, the regulations state that you could actually use the registry to provide additional coverage criterion, much

of what's been discussed today, talking about the smoking status, not just smoking yes-no, which is what the standard of meaningful use is, but 30 pack-years or 50 pack-years or whatever, in order to capture that information for coverage, an additional determination of coverages, this type of registry could be used.

So I think those are all good things that are moving in that direction. I think there's a lot of them on the ACR side, I already pointed this out around algorithmically defined followup, the stuff we saw from Lahey showed that very nicely, it was a lot of boxes, it looked complicated, but it showed that some

of this could be codified, and I think those are all sort of things in the right direction.

I've asked for recognition of centers, I take Chris Berg's earlier point that the right dichotomy of centers that have adequate expertise and breadth to do this, not a place that just has residents and so therefore is an academic medical center, is that important. And I take Doug's point as well, the surgical mortality rates nationally are much higher than

they are in places of expertise like the University of Washington, where Doug practices, and that's an important thing to think about, particularly when we're intervening on patients who are otherwise healthy and we're leading them down a medical road.

DR. MULSHINE: Jim Mulshine. At Rush we're a member of a course that supported CELN, that is capturing data on outcomes for a variety of things, and they have a funded mandate to look at outcomes in preventive services, and they're very interested in doing things, if fact we will be talking to Dr. Selby in the next couple weeks to at least talk about the possibility of integrating the concerns

that have been expressed here with a national infrastructure that's already been developed to keep track of these things.

DR. MOCK: Dr. Redberg, there still -- this is Curtis Mock. There still seems to be some confusion and I wonder if we could clarify it before we move on. Even though there's an interest to move forward to identify those that are screened, there still is some

misunderstanding about whether the follow-up radiation exposure is the same as that of the low-dose or whether it's higher. And not being certain about how many scans the patients get in followup before they drop back into the screening. I'm getting two different answers and I want to clarify that.

DR. REDBERG: Well, I think some of the data from the NLST, it was sort of all over the place, and a lot of the followups were full chest CTs that were reported at higher doses, eight millisieverts, and I'm certain that in actual practice it will be even more variable and at higher doses.

DR. MOCK: That's good enough for me, thank you.

DR. KAZEROONI: Can I just say because of the reduction in false positives in LungRADS, fewer people were required to have CTs, so the people who do require --

DR. REDBERG: Dr. Kazerooni, you haven't actually shown us any data from LungRADS, so that's why I'd prefer to keep discussing the evidence. We look forward to

seeing data from --

DR. KAZEROONI: LungRADS is already available in the ELCAP analysis.

DR. REDBERG: And you've given us those references?

DR. KAZEROONI: I think we have much of it in the USPSTF references already, from which we've extrapolated data and developed LungRADS. It means that the follow-up CTs will all be low-dose CTs, except for the two percent that are at the very highest risk for cancer who may undergo more aggressive diagnostic therapy, and that is a very important point. Most people with a positive CT who need a follow-up test will get a low-dose CT.

DR. REDBERG: My understanding is you will get the same CT that you got that showed

the nodule in the first place but you will just wait over time, and while you're waiting over time, it's unclear whether you have cancer or not, so there's a lot of uncertainty and anxiety associated with that.

Did you have a new point, Dr. Henschke, because otherwise I'd like to

thank the presenters.

DR. HENSCHKE: I just wanted to say that in specifically asking for a low-dose follow-up CT, one, if there's no growth then you go to the next annual screening, and that has not created a lot of anxiety in all the patients we've done. You have to talk to the patients.

DR. REDBERG: I would love to see the quality of life data from the NLST.

So, I want to thank all of the presenters, we appreciate your time, we have listened carefully.

And we now have a little bit of time left for discussion among the panel, so I will open it for discussion among the panel, and in particular, as you can tell, I'm interested in discussing a little bit more about the harms of

screening because I don't feel that I understand fully, you know, from the NLST as we talked about the quality of life. I'm looking now at, I believe it was called the Harms of Screening, but it had applications to lung cancer screening, from Russ Harris, published

in Internal Medicine, who was a former member of the U.S. Preventive Services Task Force.

So among other things, he notes that twice as many NLST participants in the screening arm experienced a serious complication from their workup as had their lives extended by screening. And then there is also the discussion of the psychological harms in the waiting and the follow-up procedures, all of which I think were fairly low in the NLST, but again in actual practice we know that things are not like in clinical trials, and that people seem to get more testing and less careful inclusion in screening studies.

And so I'm concerned that we haven't really explored the harms, and in particular in the Medicare population, the data that Dr. Bach told us was very inconsistent, and I personally couldn't understand the data that the model was

based on from reading the task force statement, which I did carefully. But I do know that the all-cause mortality does increase as one gets older and that in general the benefits of early detection tend to disappear as you get older

because there are more competing causes of death.

And so I am concerned that we don't really have much relevant data in the Medicare population, certainly not in the 75 to 80, and particularly on the harms, with the age group that was included in the NLST.

DR. MOCK: I have another concern about the financial comments that were made. It seems as though there might be some lack of detail around the specificity that came to the dollar per year of life saved. I'm not clear on that, I did hear the figure, but I didn't hear the standardization upon which that calculation was based. Maybe someone else on the panel can help me understand that better.

DR. REDBERG: We're really, I think, concentrating on clinical effectiveness, we're really not -- you know, while Medicare is allowed to consider costs, I don't think that

is our focus.

DR. MOCK: I didn't want that figure to get out after today's discussion without comment.

DR. GOULD: So, can I just point out that my understanding is that there is an NLST cost effectiveness analysis but that it has not yet been published, so we don't have that information at this point.

DR. REDBERG: Thank you. Dr. Woolf.

DR. WOOLF: Yeah, I wanted to build off of your comment, and begin by saying that my understanding is that the starting point for this entire NCD is the task force recommendation. I mentioned at the introduction that I spent 16 years with the task force and I have to say that in my day, looking at the evidence that's been presented, this would not have received a B recommendation, it probably would have gotten an I recommendation, maybe a C. And the task force concluded that the B recommendation was appropriate, because it reached the conclusion that the net benefit, that the benefit minus harms was substantial.

Now we can talk, and I'm sure we will, about the applicability of extrapolation to older age groups and so forth, but even if we

just stick to the data, the only evidence that the task force relied on in making this recommendation was one trial. Granted, it was a very good trial, but it was one trial, and a modeling study. And you know, the other major cancer treatments that have been implemented in the United States and in other countries have been the subjects of multiple randomized controlled trials, mammography, colorectal cancer screening and others, we have never relied on a single randomized controlled trial for setting policy for cancer screening.

But even if we throw that out the window and say we believe so much in this trial that we're willing to set policy on the basis of it, if you look at the data, I'm not understanding where we get substantial net benefit. And I wanted to ask this when our presenters could clarify it, but if you look at the 2011 paper, the 20 percent reduction in mortality from lung cancer in the 26,000 or so people that were screened, amounted to 83

asserted deaths, so you had that on one side of the scale, the 83 asserted deaths.

On the other side of the scale in terms of potential harms, and this, again, is looking at the actual data from the study. Unknown amount of anxiety, that data is pending, so the psychological harms we are not going to know about. 10,246 imaging studies, 322 surgeons that came to sign up, 671 bronchoscopies, 713 surgical procedures, 228 patients with complications, 86 of those major complications, and 16 reactogenic deaths.

So whether that represents a close call or a leaning towards benefit is something we could discuss. There is not a common metric that was used to actually weigh whether there was net benefit or net harm, that's often very difficult to do, but I don't see how you come away from that even with the NLST sample with substantial net benefit.

Add to that the additional issues we're facing when thinking about older population, different risk-benefit ratios, and lots of other considerations we'll get into about the hazards of extrapolation, and I

really don't see where we get substantial net

benefit there, but I'm interested in other panel members to reflect on, because I think that's question one that we're supposed to vote on, how they look at this evidence and see evidence of substantial net benefit.

DR. REDBERG: Dr. Gould.

DR. GOULD: Yes, thank you for sharing that. So, I want to address some of those points. I think for the most part you've raised some interesting issues. One, I want to acknowledge certainly the people who are in the room who took part and helped execute the NLST. It was a triumph of clinical science, it was an unbelievably audacious undertaking and it succeeded in creating a primary endpoint, and I think they should be publicly recognized for that.

I think -- we're not going to have another NLST. We do have the smaller European studies that may help to shed some light on this, but I think the NLST is our last best hope for RCT evidence regarding the benefits and harms of CT screening. There are certainly some things we can learn about implementation

of screening practice that we could learn from uncontrolled studies and registries and whatnot.

I think the balance of benefits and harms is really not clear, and I think this, you know, I think we're accustomed to living in a world where we make recommendations for screening interventions that are either thumbs up or thumbs down, and one size fits all, and everyone should do it, and then we, you know, have the Postal Service create a stamp so that everybody knows to get their PSA -- well, not anymore -- or their mammogram -- well, maybe not anymore.

And for lung cancer screening, here we have kind of the poster child for a situation where every individual has to weigh benefits and harms. And how you make those tradeoffs, three fewer deaths per thousand people who undergo screening, if you're at average risk, and risk is not average, none of us are average, and how do you weigh that against the false positives, the followups, the psychological harms, the biopsy procedures, that's a very personal tradeoff that people

will have to make with their physicians. I would say that would be a mistake to not allow people to have that conversation and decide for themselves, but I can see how, you know, others might be swayed.

DR. REDBERG: I think those are good points. I would say I hope we've learned something from our prior experience, because I think it's very hard for people to understand the nuances of cancer screening outcomes without a harms and benefits discussion. When you look at PSA, and I would say it's certainly not a model, you know, we now say a lot of men are being harmed, there's no net benefit and, you know, Medicare is still paying lots of doctors who are doing it every day to lots of people.

Or look at mammography, you know, what happened is the task force tried to pull back the 40- to 50-year-old group and say there were more harms than benefits. That's a hard message to get, I'm not saying we can't get it but I'm saying we should get it right, because it's very confusing to people, it's a very tricky message, and I think it is very

important for us when we make decisions and recommendations to go with this screening to have good confidence in the evidence.

DR. WOOLF: Could I respond just briefly?

DR. REDBERG: Yes, Dr. Woolf.

DR. WOOLF: When you evaluate a screening test there's five things you want to look for. First is burden of suffering; second is the performance characteristics of the screening test; third is the effectiveness of early detection; fourth is the harms; and then finally, the balance of benefits and harms. On the first point, no one in this room debates the burden of suffering so clearly we have, you know, the leading cause of cancer deaths, a major public health problem. And on the second point, the effectiveness of early detection, I would even concede that the numbers needed to screen that were published in the NLST are superior to what we see for mammography and colorectal cancer screening, that's a very favorable ratio.

The challenge I see is that the poor performance characteristics of the test with a

very low positive predictive value, and the necessity that the screening population therefore undergo not only follow-up testing but a certain subset undergoing potentially harmful and dangerous invasive procedures shifts that benefit-risk ratio in a way that we don't see from mammography screening or other types of screening tests. That in this particular case, in a highly controlled setting of the NLST, you could argue that the numbers I just read out tip in the favorable direction, and that Dr. Gould is correct in saying well, let's let that option be available to patients.

But if those risk stratification criteria start slipping, and experience has taught us that they will, then one wonders whether the risk-benefit ratio starts slipping the other way, and we as a society are offering a screening test than causes more harm than good, and therefore, it becomes a public health duty to think about the appropriateness of that.

If you argue that in addition to the NLST there is a CISNET model that the task

force based its recommendations on, I just want

to read into the record the numbers from the CISNET model that the task force based its recommendations on. If you look at the table that the task force cited in the particular row that is the basis for the 30 pack-years and 15-year quitting criteria, under that model, out of 286,000 patients that would be screened in the hypothetical model, 521 lung cancer deaths would be averted. So again, I put that on one side of the equation, and the morbidity benefits of reduced burden of suffering in terms of severity of illness that the patients would benefit from as well, so that all goes on one side.

On the other side, for the 286,000 minus 521 people that don't end up having death from the disease, 19 percent of the population is exposed to screening, approximately 25 percent will need a workup based on the NLST data, and I understand the cutoff might be different with other protocols, but under their model, this is the model the task force based its recommendations on, 1,359 patients would

have major complications, and there would be 253 reactogenic deaths plus 24

radiation-induced deaths, for a total of 277 deaths caused by screening, up against the 521 deaths averted by screening. So again, that's in the idealized risk group that the task force is specifying.

Our ability as a health care system to ensure that all patients offered CT screening will fall into that narrow band, to believe that you will succeed in doing that is naive based on the years of experience we've had with the implementation of evidence-based interventions.

DR. REDBERG: Thank you. Any other comments? Art Sedrakyan.

DR. SEDRAKYAN: I'm less concerned about one trial that is forming our decision-making. I think what I'm more concerned about is really that we don't have a very clear understanding of patient centeredness here. I think we really have a very large population in this trial and we cannot come up with the groups of risk, and

I've seen that in some of your presentations, highest quartile of risk, but I didn't see a specific characteristic of patients,

radiologists, characteristics that would help us to get more confidence about the population that is more likely to benefit from this than the other population. That's one concern I have.

I wish we would have a bit more information about the highest risk group that is way more likely to benefit than others, it would help us certainly have more positive feelings about this test, particularly in light of other data that is going to come from Europe, and would help us certainly to weight and understand what the evidence of how, if evidence is evolving as more data is accumulating, and we'll have more confidence about the larger population, rather than the specific population at highest risk.

Secondly, I think what I'm also less concerned about is whether these particular screening technologies have more advantages than mammography or colorectal. Just to

reflect on that, I think in the past ten years, the way we judge the benefits and harms have changed. Remember, ten years ago I would read publications about benefits and harms related

to mammography, and it was about arguing for this frequency-based approach, how many people get screened, how many people get benefits and how many people are harmed, and it wasn't the mainstream thinking ten years ago. While today, you see how great the presentations were about the specific benefits and the frequency, and the discussion we're having today is also reflective of our better judgments and understanding of how to balance the benefits and harms for tests like this.

So, I also, another point that I wanted to make about the small positive predictive value here, so we have seen data that says out of 21, 19 will be false positive, only one will have cancer, but then there's a workup involved there. And in the trial, about six percent of patients didn't get the appropriate workup, or the workups potentially were not related to cancer.

Now, can these percentages be seen in the real world population? It appears that it's very possible, because we already know the characteristics of the radiologists that can help us keep this at this level or higher. So

we heard a pushback from you about an academic setting or a teaching hospital setting, or any facility standards, so ideally I would like to see also that kind of information to help us make the decision.

DR. REDBERG: Dr. Grant, and then Dr. White.

DR. GRANT: One of the difficulties I have, going back to most people's comments, is that I've always had difficulties with these USPSTF reports because, as Art was alluding to, it's just weighing frequencies. And in this case a lung cancer death averted is certainly nowhere equal to any of the, or not any, but most of the adverse consequences that are rather typically limited, and that may not be the case in a frail older individual.

So I always, I find it very hard to put the benefits and the harms on a similar

metric. That's why I asked the question early on looking for quality adjusted life years, or even just life years by age, and there's some uncertainty around how we track the benefits and, or the harms from those benefits, because the tradeoffs really are key here too for the

Medicare population where the NLST represents probably a small very, or not necessarily small, but the healthy subset, and the tradeoffs would be very different among the frail older folks, but I find this very very difficult to weigh, because the mathematics in my head just don't come naturally.

DR. REDBERG: Dr. White, I think you had a comment, or Dr. Marciniak.

DR. MARCINIAK: Going back to what Dr. Bach said earlier this morning, as I tried, looked at the juxtaposition of the numbers, a part of this was how appropriate this was in terms of net harms versus net benefits, and as an economist I started thinking about with the technology diffusion what the numbers would start to look like, and Dr. Woolf and others have made it clear that it will be increasingly

difficult to resolve the I, C or B type of rating when you look at a coverage decision, because at some point it's, you know, this will go off to a broader population of individuals and the question of certifications, and we heard from ACR, you know, it is lifting things up, but the fact of the matter is not every

person who is ACR certified will necessarily be doing a lung cancer screening test as well, so there's going to be a point that seems very large as I started to sift through this evidence in advance of coming here.

DR. REDBERG: Are there any other comments from the panel, because as Maria has kindly distributed the clickers, it seems we are getting near time for a vote. Dr. White, did you want to make a comment?

MR. WHITE: Well, we've had some discussion about the rollout from academic centers to community centers, and first I would like to say that the people talked about the equipment differences between academic and community centers, and I think that is not true. Every academic center, in most large

cities, academic centers have some fancy equipment, but they have a panoply, a spectrum of equipment that mimics to a great extent what you would find in other community hospitals in the same area. And a patient who comes in for a lung cancer, a low-dose lung cancer screening may not get the shazam automatic machine that the university just bought, they're going to

have one of the regular CT scanners, pretty much the same as they'd get down the street, so I think that really is not something that we need to worry about.

I'd also say that we talked about low quality scanners and access. I think it's important, and this is an opinion, I don't have a publication on this, but 30 years experience in a state that has both rural hospitals and city hospitals, almost all of the low quality CT imaging devices are in urban areas, without a doubt. Small rural hospitals can't afford generally to have a junk CT scanner, but urban areas that have a hospital where they have three or four and one is the low quality, or referral patterns in a large city can be such

that in a freestanding center the center may not need to have high quality equipment, so I think the rural-big city distinction is also incorrect.

It's not necessary to have the lowest dose of all contemporary equipment. I think it's only important to have a dose that is low enough so that the dose doesn't matter, and I think what I've heard today is that that's the

case, or easily achievable.

And lastly, I would like to say something about the importance, if this were to be paid for by Medicare, it is really important that all Medicare patients can be confident that they're going to have a quality low-dose CT experience, comparable to what we heard described in the one study with 50,000 people, we want that to roll out to everyone, what level of quality is acceptable, only the best for Medicare patients.

And the only way to do that, and I am deeply respectful to voluntary programs, but the only way to do that is through mandatory programs where CMS doesn't pay the bill unless

you meet an accreditation standard. And we currently have that through MIPPA with three accreditation organizations, and I think it's the thing to tie this down in terms of quality is for CMS to require in some way, we don't get to vote on this, but in some way that if someone is going to get paid for a low-dose CT scan, one is accredited for a low-dose CT scan, and that needs to be not just on the MIPPA side for freestanding centers but on the other side

for hospitals as well, because currently only freestanding centers are required to be accredited by Medicare for these, hospitals get a pass. So I think quality can be had, but it's not going to happen on a voluntary basis.

DR. REDBERG: And Dr. Burke, you have the last but not least comment.

DR. BURKE: I just have a few very brief comments. First, it's very important that we don't get it wrong now, because it will be very hard to get it right later, and once technology gets established in screening, it's very very difficult to, if new technology came along, it would be very very difficult, or if

we found that this screening wasn't right, it would be very very difficult to change it. Like PSA screening, once it's in, it's hard to get it out.

DR. REDBERG: Not to mention the investment in capital.

DR. BURKE: Yeah, everyone wants to amortize their machines, and CMS expects a 95 percent amortization of the machines, so okay.

And I heard a lot about registries but I didn't hear about who's going to create it,

who's going to run it, or more importantly, who's going to pay for it, nobody volunteered and said we're going to pay for the registry. I didn't hear who's going to control it, and I didn't hear who's going to require that everyone use it. And without all of those things being in place, I just don't see that as a very viable situation.

Yeah, the study is an ideal world study, and I agree with my colleagues that weighing the risks and benefits is very difficult, especially in the context of cancer centers that really do a really really great

job, as we all know, of screening and followup, which is equally important to this whole thing, because it does no good screening these people and then they don't come back, and treatment. And whether community hospitals can function at a level of a comprehensive cancer center I think is, may or may not be an open question.

I think that we haven't said much about life expectancy of smokers, but I think Dr. Bach had a slide that said that at 55 they had a ten-year life expectancy, at 80 they had a four-year life expectancy, and this is just

smokers, that's not high risk, that's just smokers, and I'm going to assume that the high risk people my colleague is looking for, Art is looking for, are going to have a much lower life expectancy than this population, which I think complicates the whole issue of looking for high risk people if they have a low life expectancy.

The otherwise healthy patient thing, we hear this all the time, well, if they're otherwise healthy patients. Who in this population, who's an otherwise healthy patient?

I mean, how many COPD patients are otherwise healthy patients? Not very many, okay? So I take umbrage at pointing out that in otherwise healthy patients this is what it's going to look like.

And just a word about the radiation. We really don't know what low-dose repetitive radiation exposures will look like over 25 years. Most of the literature is done on single dose effects, not repetitive doses over time, which can be very difficult, and we're seeing it in animal models right now because it goes much quicker. But also, I just wonder if

these people are genetically at high risk for lung cancer, in other words, if many of these people are predisposed to lung cancer, and if you radiate them over and over again for 25 years, I'm not sure what's going to happen to them.

And finally, what kind of life? If we wait 15 years, it won't be an issue because if we start screening at 50, by the time they get to 65 they've already been screened for 15 years, so it will probably be a moot point. So

all we have to do is wait 15 years, and it will basically be a moot point what we decide.

But coming on to the main point, so, Dr. Pinsky was very nice to give me this study, and I'm sorry I nailed him about it, but you know, that's the nature of the beast here because we're talking about, the question we have to answer is in the Medicare population, not an extrapolation from some other population, right? We're not extrapolating from 50 to 65-year-olds to see what's going to happen. What is the evidence in the Medicare population?

And in fact this study, the NLST has

evidence bearing on this issue. They looked at patients 65 and older and found no significant effect. So when somebody asks me, is there adequate evidence in the Medicare population, I have no evidence in the Medicare population presented today.

DR. SEDRAKYAN: Just to correct what I said by high risk, I meant the group that was more likely to benefit, rather than the highest risk of more likely to die because of it.

DR. BURKE: Thank you.

DR. REDBERG: Dr. Howard, did you want to address the last comment, which would now be the next to last comment?

DR. HOWARD: Dr. Woolf, you brought up a lot of good points on a lot of the patients in the control arm of the trial and what were classified as intermediate adverse events. I was looking in the trial and they don't describe what that is until the appendix, and I don't have access to the appendix. Can you give us an idea, or do you know what we are talking about here when we say an intermediate adverse event with this?

DR. WOOLF: Pneumothorax requiring a

chest tube without severe adverse effects are intermediate.

DR. REDBERG: Okay. Well, I think we have now heard a good summary of the evidence, what we know, what we would still like to know and what the remaining questions are, and it's now time for the vote, so I am going to read the voting questions. Dr. Gould, did you have an urgent comment?

DR. GOULD: Well, I did want to follow up on Dr. Burke's last comment. And actually I appreciate your comments in general, I think you make some excellent points, but at least I'm going to agree to disagree about the interpretation of the evidence vis-a-vis 65 and older. I think they looked for a specifically significant interaction, they didn't find it, and you know, you can disagree with the rules, but by the rules of evidence-based medicine --

DR. REDBERG: Okay. That is why I'm calling the vote.

DR. WOOLF: I just wanted to document, I don't want to hold us up but --

DR. REDBERG: No.

DR. WOOLF: I just wanted to document

that I have additional concerns that we're not discussing.

DR. REDBERG: Okay. Well, we will have time, because after the panel all votes, I will ask each of you to state how you voted and give the reasons for the vote.

So the voting -- and just to remind you, the score that we use is, one you have low

or no confidence, and five you have high confidence, three would be intermediate, and you can vote one, two, three, four or five, only whole numbers. Okay.

How confident are you that there is adequate evidence to determine if the benefits outweigh the harms of lung cancer screening with low-dose CT, defined as CT acquisition variable set to reduce exposure to an average effective dose of 1.5 millisieverts, in the Medicare population? So again, how confident are you there is adequate evidence to determine the benefits outweigh the harms of low-dose lung cancer screening in the Medicare population? You can click now.

(The panel voted and votes were recorded by staff.)

DR. REDBERG: Okay. So the vote on that was a mean of 2.22, so that is a low to intermediate, and I will just note that that means we're not going to go on to a, b and c, so we can now go on, and I don't vote.

DR. SEDRAKYAN: So, I voted three, and the reason I voted three, despite my

uncertainty related to the overall population, I do believe there is a very large subgroup of patients enrolled in this trial and eligible for the screening that would substantially benefit from this technology. We just need to report it and find the subgroup, and maybe with future research, but I think it's really something that should have been part of our discussions today based on evidence.

DR. REDBERG: And I just reminded you, Dr. Sedrakyan, to state your name before you give your comments.

DR. SEDRAKYAN: Art Sedrakyan.

DR. FENDRICK: Fendrick, two. No comments.

DR. BURKE: Harry Burke, I voted one, and I think I stated my reasons. I didn't see any significant benefit to the Medicare

population.

DR. GRANT: This is Mark Grant, I voted a three. I think that it's a simple question obviously because the Medicare population is a fairly heterogenous one, but the representativeness vis-a-vis the NLST is

really a critical issue and I'm not entirely convinced of that as extrapolating to that population. Nevertheless, I do believe in my assessment of the evidence the NLST in terms of the relative benefit and harm, that there's a substantial portion of the Medicare population that could achieve benefit, albeit recognizing there are significant tradeoffs here and those decisions really should be made on individuals.

DR. HIATT: I'm Jo Carol Hiatt, I voted two, and actually similar thoughts as Mark's, but I got stuck on adequate, and I just didn't feel that there is really adequate evidence at this time, and it's promising, but we certainly need more information before making a broad statement about benefits to the Medicare population.

DR. HOWARD: This is David Howard, I voted a three. I recognize that there are

limitations associated with the trial and screening in general voiced by other panelists. I'm a bit concerned, the mantra of the evidence-based medicine group has always been the use of testing new technology in high

quality multicenter randomized trials, and in this case we have a large multicenter trial that showed evidence of mortality reduction, so I just worry that we might be setting the threshold so high that new technology, that no new technology can pass, at least no new medical technology in 2014, so it's just in recognition of the fact that these high quality trials exist.

DR. MELKUS: Gail Melkus, I voted a one, and maybe I was very literal in reading adequate evidence and harms versus benefits in this population, the Medicare population, which was a sharp distinction.

DR. MOCK: This is Curtis Mock, I voted a one, and the reason is that I think it's almost impossible to extrapolate to the Medicare population the expected results that we would get, when I feel it's our obligation to first do no harm. I didn't find it, I

thought I would today, and I didn't hear that the evidence is there to support benefit beyond harm.

MR. WHITE: Gerald White. I voted a

four, I thought three, I struggled with three. I thought that three was too wishy washy, I felt I had to make a stand one way or another. I think that this was a trial that is not going to be repeated, it's unlikely that we will get a better trial. So focusing on the word adequate, I thought that we should accept the results of this trial as have been previously described, because I don't think there is ever going to be something that is more adequate.

DR. MARCINIAK: Martin Marciniak. I voted three for reasons that Dr. Sedrakyan and Dr. Howard already stated.

DR. DORIA-ROSE: I voted a three as well, I --

DR. REDBERG: State your name.

DR. DORIA-ROSE: Sorry, Paul Doria-Rose. I voted a three as well, and I think my main, I would echo the same comments about I believe strongly that there is a subgroup who would benefit, it's a matter of

finding this subgroup.

DR. GOULD: Michael Gould. As a nonvoting member I voted three, and my main

rationale for that is that the issue of generalizability specifically regarding harms to settings outside of the NLST in the Medicare population, I think the rule of thumb should be to generalize beyond the trial unless there's a good reason not to, and I think the Medicare population in the settings outside of the trial are substantially different than what we saw in the trial, and I would like to see more evidence from future observational studies before I can be certain.

DR. RICH: Jeff Rich. I also voted a three for many of the same reasons here, but for an additional reason. I think we saw a lot on the benefit side, and the harm side seemed to bother everybody, but I want to remind you this is a clinical trial, and clinical trials act differently with patient outcomes than with real life data, and I think Dr. Wood made the comment that we're just learning how to handle these nodules, do they need to be biopsied, do they need to be removed. So I think there's a

learning curve here and I think that the harmful side that we've seen is probably going

to go away, or at least be very diminished over time. I did like the technology, and I think we should extend this to the Medicare population.

DR. WOOLF: Steve Woolf, I voted one. My reasons are similar to my colleagues and comments I made earlier about questions about whether the magnitude of benefit observed in the NLST is generalizable to the other populations, and concerns about whether the harms could potentially offset some of those benefits, especially if screening extends beyond the narrow risk group that the recommendation applies to.

The point I wanted to reinforce that my colleagues made is that it's not realistic to expect lots of NLSTs to get conducted, we're probably not going to get a better randomized trial than the one we have. But the solution to that is modeling, but those of you who've studied modeling understand that when you see one model, you've seen one model, and that the CISNET model is very interesting, very

sophisticated, very informative, but we can

cite many examples of other cancer screening tests where modeling studies over the years have reached different conclusions based on different assumptions that go into the model, different types of models, simulation models, agent-based models and so forth. And I think the literature, the more modeling that is done on this type of screening, we will continue to see a more diverse set of outcomes and results than what we've seen now.

I'd take advice from the chair. I have a series of concerns about challenges that we might face if CMS were to cover this in trying to replicate the conditions in the recommendations. Should I list those, or in the interest of time, do you want to just move on?

DR. REDBERG: If you want to list those, feel free, and it can be for the record.

DR. WOOLF: Okay. For the record, and I apologize to everybody for listening to this, but the recommendations from the task force that are the basis for this NCD specify that screening be offered within certain parameters,

and if you look closely at those parameters, I see implementation challenges in keeping to that risk group, both in terms of the feasibility that practices will face in actually following through on this, and we have plenty of experience in health care to know that these challenges are real, and the tendency is for those criteria to slip, and that means a lower risk group will end up getting screened and the risk-benefit relationship that we are basing this recommendation on will no longer apply.

First of all, the age group. It's supposed to be at age 55 to age 80, but we already know from discussions today that there is a sentiment to move that to an earlier age group, to start screening earlier. And also, we've heard comments made about the inappropriateness of cutting off screening at the proposed stopping age, so it's quite likely that it would not be limited to that age group.

The 30 pack-year and the 15-year quit rule, operationally, pragmatically the implementation of that will be challenging because of difficulties with screening and

intake. We have heard testimony from centers of excellence that have developed systems for doing this, and I applaud them for it, but the feasibility of expecting that to be done nationwide with implementation of this coverage policy are quite challenging. Plus, there is a strong sentiment from many of the organizations that testified today and others to loosen those criteria and accept a 20 pack-year history and so forth. And Dr. Bach noted that when you do that, the number needed to screen now shoots up to 3,000, and the whole risk-benefit ratio potentially starts changing.

A detail, a nuance in the task force recommendation that no one has discussed today is the provision that this only be done for people who are able and willing to have curative surgery. Those are two different things, but we haven't discussed either of them. How will we define who is able to have curative surgery? We've had some surgeons indicate today that there's hardly any patient who would not be eligible for curative surgery. And even those who are considered clinically appropriate for the surgery, willingness to

have surgery once informed of the potential consequences, how will that actually be implemented?

Challenges to image interpretation, I won't belabor that because I think we've had a lot of discussion about how we will implement a policy of ensuring that all radiographic facilities that are doing low-dose CT screening will adhere to the criteria of the NLST and there are wonderful efforts we've heard about today from the professional societies trying to make this happen. Most sound like they are going to be voluntary, and I agree with my colleagues that the only way to actually make, set limits on a runaway problem like we've had with other forms of cancer screening is to tie reimbursement to that, so that coverage would not be possible unless there was documentation that those criteria were being met.

The concern has been raised that if we limit screening only to facilities that are state of the art such as those at academic centers or even community-based facilities that are state of the art, we are contributing to health inequalities because so much of the

population, especially geographic areas at high risk for lung cancer don't have access to those facilities. That argument only holds if one accepts the premise that screening results in more benefit than harm. Screening done poorly, if one holds to the premise that screening done poorly results in more harm than good, then one is actually committing an ethical error by exposing disadvantaged populations or people who are disadvantaged geographically to a form of imaging or follow-up workups that are actually going to cause more deaths or cause more adverse outcomes than benefits, and that is equally troubling ethically as the barriers to access.

Another concern is whether clinicians will actually wait for the annual interval. We have time and time again with other forms of cancer screening, Pap smears and many others we could mention, where recommended intervals for screening have had a slippery slope and there's been a creep in the interval or frequency of screening that I think will be hard to adhere to.

Another topic we haven't discussed

today is the 95 percent adherence rate in the NLST. Our ability to ensure that the millions of Americans who would be offered this form of screening will achieve 95 percent adherence, a rate that I have not seen achieved for other forms of cancer screening, is very doubtful, especially when one considers that that 95 percent was achieved in a population that had higher socioeconomic status, higher educational attainment, and a younger age than the population that would actually be receiving this screening. There's reason to believe that lower SES patients and older patients might face more barriers in actually following through on the recommended protocol.

Will treatment in the community follow the same protocol? We've seen evidence presented of wide variations even within the NLST centers, the centers of excellence. It's only reasonable to assume that there would continue to be variation in widespread population use, and even worse potentially.

And then the point made about the

surgical complication rate, the very good results that were observed in the NLST, and if

I understood correctly from the NLST paper and Dr. Bach's testimony and so forth, the complication rate was one-quarter of what's typically reported. So again, when we're talking about a very tenuous risk-benefit ratio, I think these substantial differences in outcomes could tip the scales in the wrong direction. Thank you.

DR. REDBERG: Thank you, Dr. Woolf, and that was very long and thorough, but I will add, because it reminded me of two specific examples, and it's not really lung cancer-specific, but more in line with the coverage, specifically more Medicare specific, but when there is for example cancer screening in colonoscopy, we know there was a study by James Goodwin looking at the Medicare population where colonoscopy is supposed to occur every ten years unless there is evidence of a problem, but Medicare routinely paid for colonoscopy at intervals much closer to three to five to seven years, and so it is, I think,

hard in actual practice for Medicare to follow its own guidelines on cancer screening intervals.

And similarly, for a different national coverage decision with the ICDs there was a study published in JAMA looking at the data registry that was mandated by CMS with that coverage decision, that found more than one in five ICDs were put in in contradiction to the actual Medicare guidelines, and the guidelines were set up because they were appropriately defined populations where benefits would exceed harms. So I do see this as, unfortunately, a bigger issue than for this committee to deal with, but the issue that it does seem hard for the criteria that clearly defines benefits and harms to actually occur in practice for Medicare beneficiaries.

So with that, we will move on to the second question, and I will just read that again, and I was trying to get some music, which I'll work on. How confident are you that the harms of lung cancer screening with low-dose CT, average effective dose of 1.5

millisieverts, if implemented in the Medicare population will be minimized? And then there are some questions for discussion but we'll get to the discussion after the vote. So, we're

voting now on the question of how confident are you that the harms of lung cancer screening with low-dose CT in the Medicare population will be minimized, and again, it's a one to five vote.

(The panel voted and votes were recorded by staff.)

DR. REDBERG: Okay. So, the vote on that was 2.33, so again, a low to intermediate confidence vote, and we do have time for discussion, and I will just point out to you that the discussion questions to consider when you talk about your vote, which are: What harms are likely to be relevant in the Medicare population, including A, harms from the low-dose CT itself; harms from the follow-up diagnostic evaluation of findings in the lungs and incidental findings outside of the lungs; and C, harms from treatment arising from positive and false positive results? What

provider and facility criteria or protocols are helpful in minimizing harms? Dr. Sedrakyan.

DR. SEDRAKYAN: Art Sedrakyan. I voted two. And my thoughts about minimizing harms were influenced by the mistake that

Dr. Redberg talked about, the 1.5 versus 15, and the opportunities to do mistakes, and whether we have any decision or software implemented that will be foolproof in a very busy radiology department with so many of these scans done every day, the machines never stop, and you have to recalibrate suddenly and do a low-dose CT.

Maybe I'm wrong here, but I feel like there is something here that I don't understand well, and maybe someone else on the panel can explain to me where is my mistake here, but to me it feels like the implementation from that perspective might be an issue, and the harms potentially by creating this type of decision based on the level of radiation can in fact backfire then, would end up having many people with much higher radiation than we thought would be having.

So, I also didn't feel like we had proper evidence presented to us about harms that could be minimized from the workup, and the size of the nodule was one that has been discussed, was it satisfactory, was it good enough to reduce the potential for the

appropriate procedures after the CT scan? So I wasn't confident that we heard enough and how robust this would have been in terms of criteria that would help us to make a better decision.

Those are the points that I wanted to make.

DR. FENDRICK: Mark Fendrick. I voted two. Senator Morris Udall said everything is said but not everyone has said it, so I'll say some things again in a different way. I always have problems with the language of these questions, although they are better than most, about what we mean by the Medicare population, and all my votes are divided by in the patients who you think should get this intervention, as opposed to the patients I know who will get this intervention, based on experiences that

Dr. Woolf has mentioned.

So I voted three, because I think you've done everything you can, and it's superbly done in a very narrow targeted population. But since no one was willing to voice any response to my concern that there will be tremendous off-label use, some

appropriate, some inappropriate, the harms will not be, Dr. Redberg, A, B or C, but the harm I worry about will be the intervention of this test on people for which we know nothing about the benefits and harms.

DR. BURKE: Harry Burke, and I gave it a two. I agree with my colleague, indiscriminate use could be a major harm. I think the low positive predictive value drives harm, whether as my colleagues pointed out, you can balance that harm with a benefit, it's a very difficult question, but the low predictive value is a problem.

DR. GRANT: This is Mark Grant, I voted a two, but probably looking again, I might have voted a one, because this really asks us to predict the future, which is based

on, that has a questionable, well, not complete relevance to what the future might be.

But in addition to what people have expressed throughout the discussion, the one harm that troubles me potentially the most is that the use will extend to older frail individuals who in fact, the harms will vastly outweigh any potential benefit. And as, for

example, if the NCCN guidelines are adopted and those recommendations from the NLST, there's going to be a fairly substantial creep in terms of patients that will in fact undergo screening, and that concerns me with my geriatrician's hat, because I think the detrimental effects of over-diagnosis and some of the procedural things, a chest tube in a 65-year-old that can get up and walk is one thing, but for an 80-year-old who has a difficult time getting out of a chair, it could spell substantial if not just catastrophic morbidity.

DR. HIATT: Jo Carol Hiatt, and although I'm a surgeon, I spend a lot of time with my radiology colleagues, and I want to

correct Dr. Sedrakyan's concern. The equipment is quite sophisticated. As long as the correct procedure is entered into the machine, the right protocol will follow, it's very sophisticated in that way, but that was part of the reason I was curious about could we really be sure that people weren't getting diagnostic chest imaging instead of screening with a low-dose protocol, and that is I think still in

some systems, I think that remains a risk.

I should also point out that the instructions to the jury, so to speak, before the session this morning, were that we were to assume that there would be no real conditions on these questions, that there wouldn't be registries, there wouldn't be coverage with evidence and that sort of thing, that this is a basic thing. So I read this question as not necessarily having all the quality and certification controls imposed by the ACR and other institutions, that it wouldn't necessarily be limited to certified sites, that this was basically a wide open opportunity for my vote, so I voted two.

DR. HOWARD: This is David Howard, I voted a three. While recognizing the issues with the expansion of the technology outside the study population, I would be particularly concerned about expansion to people who have fewer than 30 pack-years of smoking history.

Also, I recognize, as I think Dr. Rich said, that I do believe learning curves are real and as we gain more experience the benefit-to-harm ratio will probably become more

favorable over time, and so I think that is important to take into account.

DR. MELKUS: Gail Melkus. I voted a three for the same reasons that you just mentioned, Dr. Howard.

DR. MOCK: This is Curtis Mock. I voted a two, and the reasons are that I really think that there's positive intent. This question doesn't ask about evidence, this question asks about do I think. I do, I do think that people have positive intent, I do think there is intent to do the right thing, but I don't think we're aligned, and until we're aligned, until we have those processes in

place that Dr. Hiatt mentioned, I think it's hard for me to go higher than a two. Certainly as time goes on, when our incentives are aligned and when our outcomes are the focus, I think that we will have that process built, we'll have those protocols stabilized, and I think at that point we'll know the results and be able to launch confidently, that the Medicare population would be at lower risk.

MR. WHITE: Gerald White, I voted a three. I thought with implementation I should

take my level down one level because implementation always introduces problems and uncertainties. I think there's a lot of potential for a really high-quality Medicare implementation along some of the lines that I've described, but I'm not a hundred percent sure they have either the legislative authority or the regulatory power to or desire to do that. I do think on the other hand, there is the potential for a reduction of harm in standardization of a post-positive finding, clinical handling of the patient, which was not part of the study, and I think that has the

potential to significantly change the negative outcomes from false positives.

DR. MARCINIAK: I'm Martin Marciniak. The comment that I made earlier sort of weighs on my mind so I voted a three. I worry about rapid technology diffusion, I have a concern about that because we don't necessarily know how the net benefits versus harms are sorting themselves out yet. I voted a three because I believe that we will get there and there will be a net positive benefit, and that's how I ended up with that vote.

DR. DORIA-ROSE: This is Paul Doria-Rose, so, I voted a two, and you know, I applaud the efforts of those presenters today who have been working very earnestly to come up with protocols that decrease dose and refine our definitions of positive, and I think there's, you know, that to me is where the minimizing of harms, the ability is there, but the lower confidence is reflective of my concerns about what's going to happen in routine clinical practice.

DR. GOULD: Michael Gould, I voted

two, and essentially because of concerns about generalizability and implementation. I think this is an opportunity should a coverage decision be made to cover with evidence, and really the only possible way we're going to learn about harms in usual clinical practice is to make that kind of decision and have that kind of policy.

DR. RICH: This is Jeff Rich, I initially voted three and then I changed it to two. I think if we do this there's going to be some serious implementation problems here, and I'm worried about that. I took in this

question that we took away the benefit part of it and were left with the harm part. I want to be certain that we eliminate the harms and implement this thing right.

DR. WOOLF: Steve Woolf, I voted a two. And like my colleagues, I voted a two rather than a one because I think there's a lot of hard work going on in the professional societies and among my clinician colleagues to try to reduce the adverse effects, and I think already the rates are relatively low. The

problem that I see is that the absolute benefits are also relatively low, although there is that 20 percent reduction in mortality. If you look at the absolute benefit in the NLST there was 2.06 percent of deaths in the control group and 1.75 percent in the intervention group, so the difference I think is .31 percent, if I did the math right, of the population that benefitted. So when you're dealing with numbers that small, then complication rates that are also relatively small could actually compete with potential benefits and very slight tweaks, like quadrupling the complication rate from the

surgical procedure could really alter things. So I applaud the efforts, but I think I would have also, based on the advice to the jury ahead of time, I would have given it a higher vote if for example we knew that facilities could not be reimbursed unless they were actually collecting and documenting the data to confirm that they were achieving a certain threshold for safety.

The other thing that we haven't

discussed today is Dr. Bach's recommendation for shared decision-making. So a policy that would not allow for coverage without at least sitting down with the patients and letting them know what these numbers look like using these tools, these decision aids that are available, I think would ethically make things feel more appropriate if we are going to go forward with this policy.

DR. REDBERG: Thank you all for your thoughtful comments, and that brings us to our last voting question, which I will read. How confident are you that clinically significant evidence gaps remain regarding the use of low-dose CT, average effective dose of 1.5

millisieverts, for lung cancer screening in the Medicare population outside of clinical trials?

And I'll just remind you, this is a little different, so if you are very confident there are evidence gaps, you want to vote high, and if you think there is no evidence gaps, then you would be voting low, and you can vote.

(The panel voted and votes were recorded by staff.)

DR. REDBERG: So there was a 4.444, so that's a high confidence that there are currently significant evidence gaps regarding the use of low-dose CT. And so we now have six more discussion questions, and so when we go down the panel to talk about your vote and why you voted that way, please discuss whether these or other topics should be considered for further research. In the interest of time I'm not going to read them all, but you have them there, and you can discuss your vote and in particular whether you think there are evidence gaps in what's listed, risk factors, et cetera.

DR. SEDRAKYAN: Art Sedrakyan, I voted five. All of these are certainly important gaps and we talked about them throughout the

day. I think I would like to see maybe a discussion about which gap is going to be most critical for raising our confidence in this technology, and I think the most important gap that I see again, that we talked about before, is based on totality of the data both from this large trial, which was an excellent trial and high quality, but also the publications from

other trials, being able to come up with a cohort, a subgroup, any way you would like to call it, where we would have much higher confidence that those benefits outweigh the harms than in other subgroups.

DR. FENDRICK: Mark Fendrick, I voted a five as well. I'm looking at the six questions, and so my gaps are not about radiation dose or not about venue, I think all of those things have been very well addressed. Mine is number seven, of course to repeat again, whether we would be able to figure out that the right people get the right interventions at the right time.

And my last point I think I'll make is that one of the great positive experiences I've had sitting on this organization for quite some

time was the lung volume reduction surgery, and I think it's so much coincidental that we have the same dedicated academic and community-based surgeons who took somewhat of a mixed-up or uncertain diffusion of a technology, and through coverage with evidence development has led to a really superb and probably one of the

best examples of how we've gotten a surgery that was somewhat getting out of control to now on the basis of evidence getting only performed on people who benefit the most, so to Tamara and Rita, thank you for having me, and Art, thank you for your service. It's great having you.

DR. BURKE: It's hard to follow up on that, thanks guys. I voted a five somewhat holistically, I just think the whole thing is undetermined. I think, you know, it just has to come together a lot more than it did today. The evidence, there needs to be more evidence, better evidence, it needs to be more coherent, it needs to be integrated better, but I see a future for it but not at this time.

DR. GRANT: This is Mark Grant, I voted a five as well, and would also say that

the whole list is important, I'd just say a couple things. The first, I really would like to see the quality of life data, particularly as it pertains to the elderly population, a little bit more on functional status, and I think the psychosocial issues bear some

attention.

And the last, which is something that's not listed here but was alluded to in our discussions briefly, I really think a gap is our metric in which we discuss net benefits and harms, and I really, I think it would be very helpful if something were adopted and used that could be communicated in a transparent way that placed them all in a similar scale, albeit with all the limitations thereof, but I think it would make the conversations a little bit easier. I think it would allow quantifying uncertainty and what the value of future research might be in particular areas to reduce that uncertainty, yet throwing the balls around, it's always challenging without at least some common scale, at least for me, and I think if we used it, we would get used to it.

DR. HIATT: This is Jo Carol Hiatt. I

was struck by Dr. Bach's comment that four out of the five models are wrong and they're all different. And since the screening in the Medicare population is very largely based, especially the extended age on modeling, I

think we need to validate the model with additional data. I also think that there's an enormous opportunity to mine the data from all the scans that are done and produce perhaps something analogous to computer assisted detection in mammography, where maybe we can get much more refined in determining additional features of these nodules beyond just ground glass and size, and perhaps look at the borders, look at the real density, additional data that with thousands and thousands of these images, that we could perhaps learn something looking at them in parallel with all the electronic medical records and understanding what the various biopsies and things show, and how the patients are doing. We should get a lot better at doing the screening, so I did end up voting a five, and I think it will be exciting.

DR. HOWARD: This is David Howard. I

voted a four for the reasons that Dr. Grant has already stated.

MS. ELLIS: I have -- I apologize. Dr. Melkus had to leave early, I have her vote,

and she voted a five.

DR. MOCK: This is Curtis Mock, and I'm doubly negatively challenged. My form that I signed says four, but my button that I pushed said two, so I'm really very confident that we've not yet closed all the gaps in decreasing the risks for the Medicare population screening outside of a trial. I think it's been said repeatedly today that the structure's not in place from the certification of the screening, whether it's academic, whether it's community. I still was a little bit surprised today that St. Joe's today in Phoenix is a community hospital, but so is the hospital where I practice that has 26 beds and an ICU, they're both community hospitals, and I think the definition across the country is quite variable in that regard.

So yes, I still have concerns that there are gaps around standardization and protocols, and my vote is four.

MR. WHITE: Gerry White, I voted four also. It's tough not to vote five when somebody asks you a question, are there things

that you don't know, generally my answer is an enthusiastic yes, but I did try to pick something I think is the most important, so I voted under rule four. I think the key to making this a better process is the reduction in harm for the false positives, people who have a positive report but don't actually have lung cancer, that's where the improvements are going to lie in this process.

And I just wanted for the record to make a comment about somebody previously mentioned that we didn't know the harm from repetitive low-dose CT scans of this type. I think the answer to the question is we do know that at one or 1.5 millisieverts per year for 25 years, there is adequate data that it has no medical significance. There have been studies of large scale population in high and low background area for people who have exposures like that for their whole lives and there are no significant findings there.

DR. MARCINIAK: Martin Marciniak, I

voted a four. As previously stated, I think the most important of the points there is

number four, the net harm versus net benefits.

DR. DORIA-ROSE: Paul Doria-Rose, I voted a five, and for me the key words here were outside of a clinical trial, and you know, my feeling about the biggest thing we're dealing with is in a population with likely a much higher burden of comorbidities than the population that was included in the NLST trial, and I'm worried that the risks and benefits can be affected considerably.

DR. GOULD: Michael Gould, I voted four, it could have been a five. Looking at the list here for discussion, I think there's reasons to be concerned about the evaluation of the essential findings, whether it's going to cause more harm than good, and I think the smoking cessation data is still completely unresolved, so there's been some seminal reports of favorable behavior change, but none that has, if you look at the two controlled trials that I'm aware of, they are on either side of the issue in terms of the results.

For the record, my greatest concern

and where I think the most important gaps in

evidence are, are in the area of evaluating screening-detected lung nodules, and that is based on my experience writing about and caring for patients with incidentally detected lung nodules, and their problems for 30, 40 years.

In addition, people have mentioned the NCCN guidelines for nodule evaluation. The ACCP also has guidelines for nodule evaluation, the first edition of the ACCP guidelines was published in 2003, and the second and third editions were published in 2007 and 2013. I chaired the nodule evaluation group for ACCP. We made 29 recommendations, and in the most recent third edition of the guidelines, 27 of those recommendations were weak recommendations based on low-quality evidence, so there were two C-graded recommendations. There are no randomized trials of nodule evaluation, there are no good observational controlled studies. It's a completely uncharted area and we need better evidence there.

DR. RICH: Jeff Rich, I voted a four. There are gaps, of course there are gaps, but

there are gaps in any new technology. Just look at the transcatheter aortic valve replacement; when that rolled out, there were so many gaps, but we went ahead and we wanted to get that technology out, and in fact the results post commercialization are better than they were in the clinical trial because we got smarter with time.

So here I would think that, and I just want to go on record as saying I think this is an important clinical tool for our patients, I really think that if we don't want it implemented in the entire Medicare population, I think it does need to be studied somehow, some way, in a pilot or in a registry setting with certain centers because we want to have the answer, but there is not going to be another randomized clinical trial.

DR. WOOLF: Steve Woolf, I voted a five. Most of my reasons are the same as my colleagues'. In terms of unanswered questions, in addition the ones that have been suggested, I would like to add one more, which is prudent use of resources. We need to think about if we do cover this, basically you think of it as CMS

writing a check for a strategy to reduce deaths from lung cancer that we know are largely caused by tobacco, and year after year the CDC reports significant shortfalls in funding the states for tobacco control efforts. Whether it wouldn't make sense to allocate our resources directly at tobacco control interventions where we would see absolute risk reduction that would eclipse what we're seeing with early detection of lung cancer through CT imaging.

That's not to suggest that the important findings reported by the speakers today about how CT screening might encourage people to quit smoking shouldn't be recognized and applauded, but I wonder if our dollars could go further in actually saving lives from lung cancer by dealing directly with tobacco abuse.

DR. REDBERG: Okay. I just wanted to address one of the earlier comments that was made, because there is data directly estimating the number of fatal cancers per millisievert, which is .05 fatal cancers per sievert of exposure, which means that for the NLST for what they would be expecting, one cancer death

to result per 2,500 patients who underwent three annual low-dose CT scans. So there is a number and it is more than zero, and obviously it goes on to say that if those people got diagnostic CTs, there would be one cancer death per 550 who went for three annual screenings.

But I really want to thank everyone who came today, I want to particularly thank Tamara Syrek Jensen for leading our group, Maria Ellis, my vice chair, Art Sedrakyan. I want to thank all of the presenters, the people who attended today, the public comments, and especially the committee, because I think that clearly, you know, we are in a very interesting time of trying to look at the evidence, balance harms and benefits, I think we're having really important discussions that need to be discussed, but that are really not that easy for anyone.

I think we used to think a new technology, that's good, and we're really talking a lot about what do you think the technology means, what does it mean to this particular population, what are the risks,

what are the benefits, how could it best be used, and those are really thoughtful questions, and I know everybody here has all the best intentions to do the best thing for all of our patients, or our Medicare beneficiaries in particular. We all think very highly of the NLST, it was a very well done trial, and I thank the committee for all of your work.

MS. JENSEN: Just a quick comment for some of you that are doing research in new technologies, one of the new ones is the e-cigarette, that's another gap, we have no idea what to do with those.

DR. REDBERG: So, that's a good idea for another, huh?

MS. JENSEN: So, I just want to say thank you again to the panel. I especially want to say thank you to Art, because this is his last MedCAC and then he takes a year off, so thank you for your tenure here, you've done a wonderful job.

Thank you everybody, and thank you to the speakers. I think I will be hearing from

many of you, we have a big job ahead of us, and

remember, there is another public comment period coming up as soon as we issue our proposed in mid November, so look for that.

Thank you very much.

(Whereupon, the meeting adjourned at 3:12 p.m.)