National Government Services, Inc.
Moderator: Craig Haug, MD
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Coordinator: Welcome and thank you all for standing by. At this time, all participants will be in a listen-only mode until the question-and-answer portion throughout today's conference. During the question-and-answer portion, if you would like to ask a question on the phone, you may use star 1. Today's conference is being recorded. If you have any objections, you may disconnect at this time. I would now like to turn the conference over to Dr. Craig Haug. Thank you. You may begin.

Dr. Craig Haug: Good afternoon and welcome everybody to the NGS Open Meeting.

Next slide please. This is a reminder this call is being recorded and transcribed.

Next slide. And welcome from all the NGS CMDs including doctors Awodele, Cunningham, Boren, Duerden, and McKinney.

Next slide please. The proposed policies or LCDs on the agenda for today include thyroid nodule molecular testing, respiratory pathogen panel testing, epidural procedures for pain management, non-invasive fractional flow reserve, FFR, for stable ischemic heart disease and CT tomography, CTT and coronary computed tomography angiography, CCTA.

Next slide please. The first draft under discussion is one of mine and it's thyroid nodule molecular testing. This draft was a new LCD request. And over 600,000 thyroid fine needle aspiration biopsies are performed every year in the United States

with approximately 20% classified as indeterminate. In other words, cannot absolutely determine whether it's benign or cancerous.

Previously most went on to diagnostic thyroid surgery, usually lobectomy, which most 75% to 95% ultimately confirmed to be benign. So the vast majority of those indeterminate ultimately were benign and arguably didn't require that surgery.

Molecular marker testing is a potential method to augment risk stratification in indeterminate cases, those cases we just discussed, ideally reducing the need for diagnostic thyroid surgery or complete thyroidectomy with the risks and costs.

The LCD coverage criteria in this draft are on the slide and to summarize describes those patient characteristics most likely to benefit from molecular testing, mainly indeterminate cytology in a patient with other indications for surgery who would be willing to potentially undertake surveillance should the molecular test results indicate low cancer risk.

Next slide. In summary, this coverage criteria support guideline-based molecular testing of thyroid nodules, but we also look forward to future studies that better define clinical utility especially given recent improvements in imaging and cytologic classification.

We received requests to comment on this policy. First up is Dr. Desai. Operator, can we see if Dr. Desai is available? And open his line if so.

Dr. Dimpi Desai: Yes I'm here.

Dr. Craig Haug: Excuse me?

Coordinator: Yes, Dr. Desai, your line is open.

Dr. Dimpi Desai: This is Dr. Desai. Can everyone hear me?

Dr. Craig Haug: Yes. Yes. We can hear you, Dr. Desai. Please proceed.

Dr. Dimpi Desai: Thank you. So my name is Dimpi Desai. I recently completed my endocrinology fellowship at the University of Pennsylvania a year ago where I trained with Dr. Susan Mandel, one of the world experts on thyroid nodules.

And since the year I've been working as assistant professor at Baylor College of Medicine and one of my clinical areas is thyroid nodules and thyroid cancer. And I have no conflicts of interest for today.

Next slide. So we're very excited clinicians. We're really excited to see that molecular testing for thyroid nodules is now considered medically necessary. As Dr. Haug correctly pointed that about 20% to 40% of the time we encounter this very common diagnosis of indeterminate cytology of Bethesda III and Bethesda IV where the cytology is just not clear enough to tell us benign versus malignant. And where formerly these patients would go for surgery, now we have the option of molecular testing for them.

And the topic for today is the requirement - discuss the requirement of two FNA for Bethesda III cytology before a molecular test can be done. And for that, to discuss further, I would like to talk about my studies, which I did during my fellowship a year ago, that was published at Cancer Cytopathology last year.

Next slide. So for this study our objective was to study the performance of ThyroSeq Version 3 for Bethesda III and Bethesda IV nodules. At Penn, we started using the study in December 2017 right when it came out. And for this study, I looked at data from December 2017 to August 2019 to evaluate all the nodules that underwent ThyroSeq testing at our institute.

Total, we had about 415 cases that underwent ThyroSeq testing, out of which 251 were of the class of Bethesda III and 164 were of Bethesda IV cytology. And we had surgery and pathology results available for a total of 127 nodules.

And our primary objective was to study how accurate is the test or to determine its performance in predicting the diagnosis of which of these nodules are benign, which of these nodules are malignant. We just wanted to know how good the study is by comparing the ThyroSeq results to the final pathology.

Next slide. So the first table here gives us the performance of ThyroSeq Version 3 and I'll focus on Bethesda III nodules. The sensitivity of this test was 95%, specificity 94%, negative predictive value, 99.5% and positive predictive value 61%.

I would like to focus on the negative predictive value of 99.5% for Bethesda III nodules which means that if a nodule with Bethesda III cytology result is negative on the ThyroSeq Version 3 test, there's a 99.5% chance that this is benign and hence that would reduce so many unnecessary diagnostic lobectomies or diagnostic surgeries that the patient would have otherwise gone for.

The next question is, how often are we seeing this negative result for Bethesda III? And for that, we calculated the benign call rate. And out of the 251 nodules with Bethesda III cytology, 206 were negative by ThyroSeq which means that 82% of these nodules which have Bethesda III cytology, the result comes as ThyroSeq negative and that 99.5% of these then eventually are benign on surgery which means that the benign - high benign cell rate of these tests for Bethesda III will help us to eliminate a lot of unnecessary surgeries that otherwise the patients would go for.

Secondly, out of these 206 Bethesda III nodules, 13 still underwent surgery either per patient preference or anxiety or compression symptoms. And initially one was cancer but we reviewed the pathology and then it came as benign. That is all the Bethesda III with negative ThyroSeq that underwent surgery had a benign pathology.

So we concluded that the high benign cell rate of this ThyroSeq test for Bethesda III nodules would prevent a lot of unnecessary surgeries in about 82% of patients. When a patient has a negative result on this test, the clinician as well as the patient

will believe that this nodule is benign and hence no further follow-up will be needed in terms of lobectomy or surgery.

This will improve the patient quality of life as well as the need for any further intervention. If we keep the requirement for two FNA, then that would add additional anxiety for the patient to wait another three months and then to have another FNA, which may be followed by molecular test which leads to more anxiety, more costs and then some patients may just go for diagnostic lobectomies which would actually increase their healthcare costs.

And for those reasons, I think that a negative ThyroSeq test after the first FNA for Bethesda III would really help in reducing the overall healthcare costs for thyroid nodules in Bethesda III cytology.

Thank you. And with this, I'm happy to answer any questions.

Coordinator: Thank you. We would now like to open the phone lines for any questions. On the audio side, if you would like to ask a question, please unmute your phone.

Dr. Craig Haug: This is Dr. Haug. I'll start in. Dr. Desai, thank you for these comments and also for sending me a copy of your paper. I do have a question on the data that you just showed and whether it's somewhat the numbers are a little bit more inflated than maybe they should be. The data includes 253 ThyroSeq-negative patients who did not undergo surgery. And therefore for them, there was no definitive histologic data.

Dr. Dimpi Desai: Yes.

Dr. Craig Haug: In your paper, you say that the data on all these 253 assumes in terms - for the purposes of calculation that they were called true negatives.

Dr. Dimpi Desai: Yes.

Dr. Craig Haug: In other words, no false negatives. However, there were 31 ThyroSeq negative patients that chose surgery even though they were ThyroSeq negative for various reasons.

Dr. Dimpi Desai: Right.

Dr. Craig Haug: And among these, five turned out to be malignant, which is a 16% false negative rate, far different from that 0% that's assumed for those 253. As you - and even in your paper, you have another chart or table similar to this that just looks at those 127 patients for whom histologic follow-up was available. In other words, you have a one to one match between the ThyroSeq results and actual histologic data from the surgical specimen.

And in that chart, in that table, the specificity drops from the 90% on all nodules here shown in this slide to 46% -- big difference -- and the negative - positive value drops from 98% to 84%.

So I wonder if you could comment on this.

Dr. Dimpi Desai: Yes. So to answer your first question, for the five false negative cases, four of them were Bethesda IV. And, you know, we know that Bethesda IV has a higher rate of malignancy than Bethesda III. So four were Bethesda IV and also all low risk as defined by ATA one of them was Bethesda III and then that's the one that we reviewed the pathology and there was no capsular invasion. Actually it was a follicular adenoma, not a follicular carcinoma.

So later in my paper I have discussed that, you know, initially we presented the result that yes, there were five false negatives because this is real world data. But then when we re-evaluated those five false negatives, the one with Bethesda III is actually a follicular adenoma which means that none of the Bethesda III classes had any false negative cases at the end.

And to answer your second question where we did - you know, we do - this is - and even all other studies either ThyroSeq or any other molecular testing often consider negative cases as true negatives for their practical application and real world scenario is the theme and that's what we did as well.

But when we looked at the data for just the 127 nodules for histological follow-up, if you just focus on the Bethesda III performance, then the sensitivity is the same as 95% and the specificity just dropped but the main point is the negative predictive value still stay as high at 92% and the main reason of this molecular testing is to correctly identify the benign nodules so that the unnecessary surgeries are avoided.

So even with the histologic follow-up for 127 nodules, the negative predictive value stayed at 92%.

Dr. Craig Haug: Right, which is still lower than the 99.5 in the data.

Dr. Dimpi Desai: Right.

Dr. Craig Haug: …and like I said, the specificity did drop from 94%, just sticking to the Bethesda III at least 48%. I mean, that's - I guess my basic question, is it really fair just to show data that assumes incorrectly that all those that you don't have histologic information on were true negatives when you know that that can't be true?

Dr. Dimpi Desai: Right. Right, right. But for practical - you know, for practical reasons, for all those negatives will be considered true negatives and I think long-term follow-up is lacking and definitely more studies will be needed for long-term follow-up but even if we - even if they do have malignancy in the future or they are false negative, they would be low risk by ATA.

Dr. Craig Haug: Right. Thank you. And again thank you for your comments and thank you for sending the paper so I could look at it ahead of time and congratulations on finishing your training and getting a study published on top of it.

Dr. Dimpi Desai: Thank you.

Dr. Craig Haug: Okay. The next speaker on the agenda is Dr. Hodak. Operator, can you see if Dr. Hodak - can you open his line if he's available?

Coordinator: Dr. Hodak, your line is open.

Dr. Steven Hodak: Thank you. Good afternoon. I'm delighted to have an opportunity to speak to the group today. I'm Steven Hodak. I'm a professor of medicine and endocrinology at NYU Langone Health. My practice is basically entirely related to thyroid nodules, thyroid cancer and thyroid disease.

I'm also intimately familiar with molecular diagnostic testing since in the early 2000s when I was at University of Pittsburgh, tests like ThyroSeq were just being developed that I had the opportunity to participate in much of the clinical validation of the early tests and the processes that led to what we now have available commercially in the market.

I will disclose that I've received compensation for speaking for Sonic Healthcare USA on behalf of ThyroSeq.

I will also disclose that prior to receiving that compensation, I very happily spoke on behalf of ThyroSeq because I think it's an excellent test that I find extremely helpful and useful for clinical care of my many thyroid patients.

Next slide please. There is some literature. It's limited but there is some literature that looks at this issue of outcomes when indeterminate cytology results are repeated. And I think the question at hand really is, can a discordant result, a second biopsy result that is, for instance, benign reverse or negate an initial biopsy result that is indeterminate?

I actually think that's a bad idea. I think that there's a lot of problem with light microscopic diagnosis and cytology in general in these categories of benign versus malignant are extremely fungible. There's very nice data that I don't present that

shows that when cytology cases are reviewed, opinions about what the actual gold standard diagnosis is are widely discordant. And I think it points to the fact that we are at a hard limit of what is possible with light microscopic diagnosis.

And this idea that you can get a different diagnosis from biopsying the same nodule is not a trivial issue. In this data that was presented from Memorial Sloan Kettering of a large population with about 450 patients with indeterminate AUS Bethesda III cytology, what we can see is that if you look at the second biopsy result, there was a cohort of 96 patients. Forty-three, almost forty-three percent of those patients had a second cytologic diagnosis of benign.

In my mind, this represents a problem because that means 43% of the patients that are evaluated are now in this gray zone where it's unclear whether we should believe or discount the original diagnosis of indeterminate and rely instead on the second diagnosis of benign.

I think what this would lead to for this large number of patients is more intensive follow-up, additional ultrasonography, more office visits, additional costs that I think would accrue because we are now dealing with uncertainty again rather than a definitive result.

And I believe molecular testing is a far better way to make a definitive diagnosis than - diagnosis in this case and that definitive result with molecular testing would allow us to appropriately deescalate the intensity of follow-up in many cases that I brought a case to show you that I hope will make that point.

Next slide please. So this is one of my patients, a 56-year-old man with a 4-centimeter thyroid nodule. You can see the nodule in the ultrasound. It is heterogeneous. It's fairly isoechoic. There is an irregular border. There's a large shadowing macrocalcification in the center and perhaps some small microcalcifications within the nodule. It was a solitary nodule. His regional lymph nodes were normal. He had no risk factors for thyroid cancer.

Next slide please. He had a biopsy that was done elsewhere. It was read as Bethesda III atypia of undetermined significance. And the question here is, what would be the next most appropriate step? I think the group is perhaps suggesting that repeat FNA cytology would be the right next step. I would argue that molecular diagnostic testing would be reasonable in this case.

Next slide please. So he did undergo a repeat FNA and this time it was read as benign. So if the plan would be to not advance the molecular diagnostic testing, we would stop here and then put this patient on a path where continued observation would be done. In this case, I did however get the molecular diagnostic result because I was concerned about, A, how the nodule will look and also the extent of the atypia on the original cytology.

And it was indeed positive for an ETV6-NTRK3 fusion. This is a gene fusion that conveys a very high risk of invasive thyroid cancer approaching 100%. And I think that was very useful information.

Next slide. He underwent a total thyroidectomy and he did indeed have an infiltrated, invasive, follicular variant of papillary thyroid cancer with vascular invasion. There was extra-thyroidal extension, multiple positive lymph nodes. He then underwent adjuvant radioactive iodine therapy and I just want to point out in the SPECT-CT that you see below, there's a focus of uptake in the lungs. So at initial presentation, this patient also had a lung metastasis.

Next slide please. So how does this happen? So this is a photomicrograph of the actual tumor histology and what you may be able to appreciate is that it's extremely heterogeneous. In the smaller box more to the right, you can see that the cells in that area looked dark and blue. In the larger box to the left you can see the pink colloid, typical of benign thyroid tissue with lots of very bland epithelial cells.

Tumors are heterogeneous and they are histologically not - they're not the same when you look throughout a tumor in many cases. A biopsy from this area that's

more blue from the smaller box on the right is going to produce cytology that looks overtly abnormal.

However, a biopsy from the area on the left is going to look far more normal and perhaps even benign. And this is not an infrequent finding when we evaluate thyroid tumors.

If however we were to look at the molecular diagnostic signature of the epithelial cells in both of these specimens, since we know this is a clonally neoplastic nodule, a tumor that originated from a single progenitor cell that enlarged and divided to form a clone, we know that even the areas that looked benign would have the same molecular genetic signature for cancer that the more morphologically overtly normal cells would also show.

Next slide. So I'll just conclude by saying that there is no reliable data on the safety of observation in thyroid nodules with benign cytology that follows an initial diagnosis of Bethesda III or FLUS/AUS. Repeat FNA for these Bethesda III nodules is suggested in some management guidelines but is certainly not required by any current thyroid nodule guidelines for many of the consensus organizations like American Thyroid Association, the Endocrine Society, American Association of Clinical Endocrinology, et cetera.

Repeat FNA is not required for molecular testing by other Medicare carriers and commercial payors. And I fear that if this becomes a requirement, it would complicate and delay patient access to needed care in molecular testing. It would limit the use of molecular testing and require further hardship for the patients who will have to return for second procedures in the office, take more time off work. It'll increase the anxiety and waiting. And I think all of that is relatively unnecessary because they think molecular testing represents a really excellent way of resolving these indeterminate cases.

I'll stop there and happy to take questions.

Dr. Craig Haug: Dr. Hodak, I have a question for you. You mentioned specifically that this is in - the need for a second FNA in Bethesda III isn't required by any guidelines. And I think you actually specifically cited the American Association of Endocrine Surgeons. Is that correct?

Dr. Steven Hodak: I didn't but…

Dr. Craig Haug: Okay.

Dr. Steven Hodak: I'm not actually sure what theirs are.

Dr. Craig Haug: Okay, because the 2020 American Association of Endocrine Surgeons guidelines does recommend it. They - I'll just quote their guideline. "Results in Bethesda III category nodules may undergo repeat FNAB which leads to a more definitive reclassification of 60% to 65% and thus is recommended as the next clinical management step."

So I guess from my perspective, this is somewhat at odds with your claim but I'd like to hear your thoughts.

Dr. Steven Hodak: Well, you know, my thoughts are if we follow that reasoning, this patient that I just presented with a metastatic cancer would have been dismissed as a benign biopsy as a more definitive result. I think just logically I don't…

Dr. Craig Haug: No, I understand that. But just sticking to your claim about the guidelines, I think that there are some guidelines out there that do recommend it.

((Crosstalk))

Dr. Steven Hodak: Well, I mean, if you're stating that - I mean, I'll take your word for it. I'm not familiar with their specific guideline. I know that many of these guidelines are also based on consensus and opinion and they're not, you know, soundly based on facts or evidence. And the fact is I would just wonder how it is that a second biopsy result of

benign is more definitive and more correct than an initial diagnosis that shows atypia. Does it mean the first diagnosis is incorrect or wrong?

Dr. Craig Haug: Yes, I understand that reasonable people can debate that point. I was just focusing on whether there are guidelines and I assume that that's the American Association of Endocrine Surgeons, and 2020 is a very recent and important guideline, but maybe I'm incorrect about that. Is that incorrect?

Dr. Steven Hodak: No, I don't think you're incorrect but guidelines are guidelines. They're…

Dr. Craig Haug: Okay. Yes. Okay. Yes, I just wanted to, you know, establish whether there were no guidelines or at least there were some. I just did note that the NCCN, which had until their most recent guidelines, did basically say repeat FNA for Bethesda III, and they just changed it to consider repeat FNA. So even NCCN until the very latest version 1.2021 seems to recommend a second FNA for Bethesda III also.

So anyway, that's all I had. I just wanted to ask and flush out the question. I understand there's arguments to be made for and against guidelines in general but I just wanted to establish that there are least some guidelines that do recommend it.

Dr. Hodak, thank you for your comments. I appreciate you being here today. We can move on to the next speaker I think. Next is Dr. Levine. Operator, can you see if Dr. Levine is available?

Coordinator: Dr. Levine, your line is open.

Dr. Robert Levine: Thank you. Thank you for allowing me to speak at this meeting. My name is Dr. Robert Levine and I'm a board certified endocrinologist and I'm the medical director at the Thyroid Center of New Hampshire.

I've been practicing endocrinology for over 30 years and my practice has been limited to disorders of the thyroid for over 20 years.

I was the director of the Thyroid Ultrasound and Biopsy Course for the American Association of Clinical Endocrinology between 2005 and 2015. And I've been an instructor in thyroid ultrasound and biopsy for the American Thyroid Association, the Endocrine Society and the American Association of Clinical Endocrinology for more than 15 years.

I've been an author and editor of three textbooks of thyroid ultrasound and thyroid biopsy and I've written several additional chapters on thyroid biopsy technique.

I have no conflicts of interest. I have no outside support.

I'd like to discuss the medical decision-making for thyroid nodules specifically how a Bethesda III biopsy is interpreted in relation to other information, explain why a policy of necessitating a repeat biopsy for Bethesda III cytology is clearly not in the best interest of the patient.

When evaluating a patient with a thyroid nodule, the medical decision-making involves sequential steps. Approximately 1% or 2% of thyroid nodules harbor a malignancy but all nodules are not equal. For example, patients with a strong family history of thyroid cancer or history of exposure to radiation start with a higher risk of having cancer.

All patients with a nodule should have an ultrasound and ultrasonographic findings can be either reassuring or concerning. Both the American Thyroid Association and the American College of Radiology have developed systems which assign a probability of malignancy based on the ultrasonographic features and make a determination of whether a biopsy is necessary based on that risk and the size of the nodule.

Following the biopsy, the pre-test probability of malignancy based on the ultrasound is revised and medical decision-making progresses to whether observation or surgery is most appropriate.

As we've heard, approximately 15% to 20% of the time the initial biopsy is indeterminate including both B3 and B4 lesions. In the past, most of these patients underwent diagnostic surgery but as we have heard from the prior speakers, the use of molecular markers has been shown to drastically decrease the need for diagnostic surgery.

The proposal we're discussing today would necessitate a repeat biopsy and all Bethesda III lesions prior to performing molecular markers. Clearly the only advantage of this approach is potential cost savings. When analyzing the cost savings however, it's important to consider the cost of repeat biopsy and cytology in all those cases as well as the cost of molecular markers in approximately 40% of cases.

When you add in the 5% of repeat biopsies that will be insufficient from that same paper out of Memorial, the cost savings are going to be quite small.

However, there are multiple disadvantages to this approach. From a patient viewpoint, the most important is being faced with the need for a repeat biopsy and as many as 15% to 20% of all cases. To a patient, there's a huge difference between having four needles stuck into their neck and having eight needles into their neck in two sessions.

Equally important is a three-month delay in diagnosis. Guidelines recommend that a repeat biopsy not be performed immediately as there will be regeneration artifact which will increase the false positive rate of the repeat biopsy. Recommendations for delay range from one to three months. And in my practice I waited for three months as I have had multiple cases where the repeat results were misleading after waiting a shorter time frame. That three-month delay in diagnosis gives the patient a three-month window of high anxiety regarding both the diagnosis and the upcoming procedure.

In addition, there's the possibility of disease progression if the nodule does harbor an aggressive cancer.

The need for repeat biopsy results in cost as well as inconvenience and lost time for both the patient and the provider. Perhaps the most important disadvantage to the patient of the proposed approach is the lack of predictive value that is obtained from the molecular markers. The markers not only give a probability of whether malignancy is present but also whether the lesion is likely to be a low grade, intermediate or high grade cancer. This information is extremely important in determining the extent of surgery, not just the need for surgery.

In a patient with an initial Bethesda III lesion, as Steve has told us, it's unclear how reassuring a subsequent benign biopsy will be. However, if molecular markers are performed and no mutations are present, one can certainly deescalate the intensity of future monitor.

When I am faced with a negative molecular marker profile, I am comfortable with observation. However, if a patient had an intermediate or high-risk lesion on ultrasound in an initial Bethesda III biopsy with a repeat biopsy of Bethesda II, I am not comfortable following that patient loosely and I will intensively monitor the patient with serial ultrasounds and likely even repeat a third biopsy.

Currently when I obtain informed consent prior to biopsy, the patient is told that there's approximately a 2% chance that the biopsy will be insufficient and non-diagnostic and I'll need to repeat the biopsy. Under the proposed regulation, when obtaining informed consent, I will have to tell the patient that there is a one in five chance that we will end up with a Bethesda III cytology and need to repeat the biopsy procedure.

So before I perform my first biopsy on the patient, I'll be telling them there is a one in five chance rather than a 1 in 50 chance that we will be going through the entire procedure again in the future.

While biopsy is relatively painless in good hands, it may be quite uncomfortable in others. Patient anxiety is extremely high regarding this procedure and subjecting 20% of them to a repeat biopsy is not in their best interest.

So in conclusion, medical decision-making for thyroid nodules integrates clinical parameters, ultrasound findings, cytology and molecular markers to determine both the need for surgery and the extent of surgery. The presence of a mutation in the Bethesda III nodule provides invaluable information regarding both the need for and more importantly the extent of the surgery to be done.

Requiring a second biopsy following Bethesda III cytology may save a small cost at the expense of patient inconvenience, risks to the patient and lack of extremely useful prognostic information to be gained.

Performance of molecular markers should be a decision made by the clinician based on the total information available including clinical factors, ultrasound findings, the actual cytology and the patient's concerns. And doing a repeat biopsy should be an option in medical decision-making rather than a requirement.

Dr. Craig Haug: Dr. Levine, thank you for those comments. Just one comment and then one question for me. Just to make clear, Medicare coverage doesn't include consideration of cost. And I will mention that that may be in the mix. And we're actually not allowed to include considerations of cost in our coverage determinations. Then - you mentioned that as it stands, all Bethesda III lesions require repeat testing.

At the end I think you mentioned that you think it should be an option. Can you describe the patient characteristics that would lead you to a repeat FNA rather than going right to molecular testing?

Dr. Robert Levine: There are very few situations where I would choose that as an option. However, there may be patients who - because of the cost that they may run into from copays and coinsurances say, "I would rather have it performed again." I would certainly try

and talk the patient out of it because I don't believe that it's extremely useful even when it comes back benign the second time.

There are also situations - a paper that I wrote some years ago with Dr. John Avely where we looked at artifacts that result in Bethesda III cytology and there can be caught artifact and other things that lead to a misread on those. So I look at my own cytology images provided back to me from the pathologist. And if I were looking at it and saying that it were a poor biopsy that resulted in B3 in those situations, I may go on to a repeat biopsy rather than molecular markers.

Dr. Craig Haug: So aside from cost considerations and Bethesda III inadequate FNA, you're saying, no, you wouldn't do a repeat.

Dr. Robert Levine: I didn't follow your question.

Dr. Craig Haug: Well, it seemed like the two situations you described where you might consider a repeat and molecular testing would be costs, copays, et cetera, you mentioned and also where there is the original FNA was technically inadequate. Did I have that right?

Dr. Robert Levine: Correct. Yes.

Dr. Craig Haug: Okay. So aside from that though, just other characteristics of the initial FNA or ultrasound characteristics or something, there's no other clinical criteria that would induce you to do a repeat FNA.

Dr. Robert Levine: No, there would not be.

Dr. Craig Haug: Okay. Dr. Levine, thank you for your comments and answering the questions. I find it very informative. Operator, can you see if there are any other comments on this policy?

Coordinator: Thank you. We would like to open the phone lines for any questions. If anyone does have a question, please unmute your phone, hit star 1 and record your name when prompted. Again that's star 1 to ask a question. One moment to see if we have questions on the phone. And I am currently showing no questions on the phone.

Dr. Craig Haug: Thank you Operator. So comments on this policy at this open meeting are now closed. Dr. Awodele, I believe you're up next.

Dr. (Ola Awodele): Yes. Thank you, Dr. Haug. Good afternoon. My name is Dr. (Ola Awodele) and I am the lead CMD on this next draft policy which is respiratory pathogen panel testing.

The indications we have on this draft policy are that respiratory pathogen panel testing in the outpatient Part B settings will be considered medically reasonable and necessary when all of the following are met.

One, the panel is with less than or greater - less than or equal to five respiratory pathogens are performed and both of the following criteria are met.

The outpatient setting is equipped to deliver timely results and for patients who have demonstrated that clinical management can result in an improved health outcome. So clinical utility is established.

The limitations of this policy and it's more of a place of service limitation is that the following is considered not medically reasonable and necessary. Panels with greater than five respiratory pathogens performed in the Part B outpatient setting.

A study that we reviewed for this draft LCD demonstrated that other than testing for influenza and recognition of the importance of identifying COVID-19 testing for multiple pathogens using respiratory pathogen panel test have not been proven to impact clinical decision-making, resulting in improved patient outcomes.

Therefore, we're concluding in this draft policy that respiratory pathogen panels have greater than five respiratory pathogens are not medically reasonable and necessary for the purposes of Medicare coverage. Again, this is not medically reasonable and necessary statement is in the Part B setting.

So we did have a request to give a presentation on this draft LCD.

Operator, could you see if Dr. Pritt is on the line? And if she is, if you could open up her line.

Coordinator: Yes. One moment here. And, Dr. Pritt…

Dr. Bobbi Pritt: Can you hear me?

Coordinator: …your line is open. Yes, your line is open.

Dr. Ola Awodele: His or her line. I was just about to say his or her line when I saw the spelling of "Bobbi" but okay.

Dr. Bobbi Pritt: Thank you very much. Well I appreciate the opportunity to speak to this today. My name is Dr. Pritt, Bobbi Pritt and I'm the chair of the Division of Clinical Microbiology at Mayo Clinic. I'm a board certified clinical microbiologist and pathologist.

And we do a number of multiplex respiratory panels at my laboratory. We also do more targeted assays and I am here to say that there's utility, I believe, in multiple different approaches really based on the clinical presentation and optimal test utilization.

So if you can go to the next slide please.

So I don't have any conflicts of interest. I will be discussing specifically the BioFire Respiratory Panel as that's the channel that we use in my laboratory but I don't have any financial interest or conflicts with that product.

So next slide please. So as was just nicely mentioned, we're talking about respiratory pathogen panels that detect multiple pathogens. There are now many on - well, several on the market, some of which are FDA cleared that will detect multiple pathogens within a short period of time which is very powerful to have a result within an hour or even less to be able to make decisions at a point of care setting.

So for example, the BioFire FilmArray Respiratory Panel detects 22 targets in 45 minutes. And I listed here that there is a clear wave diversion which can be done at a point of care setting. In fact, we do do that in some of our outpatient settings. It's the Respiratory 2.1-EZ detects 19 targets.

In addition to the four targets in black, which I think usually would fall into probably the five targets that this policy, the LCD is covering, there are also all the other targets in red, which are important pathogens in and of their own right. And we know of course viruses don't require antibiotic treatment where some of the bacteria do. And given our global pandemic of antimicrobial resistance testing, it's our belief that detecting of these additional pathogens is quite significant as well.

So if you go to the next slide please.

This is the NGS proposed local coverage determination. So I won't go over that again. But if you go to the next slide, I will say that the Mayo Clinic position statement is that panels with more than five respiratory pathogens are also acceptable, not just ones with less than or equal to five in the Part B outpatient setting when both of those criteria are met. Essentially that the outpatient setting is equipped to deliver timely results.

And with these tests available in one hour or even 45 minutes, it could, if designed correctly, really fulfill that requirement. And it has to be done in line with good test stewardship for patients where the test result aids clinical management.

If you go to the next slide.

So we really look at this from the whole test life cycle. The reimbursement has to be considered in the context of the entire healthcare system. And in our mind really can't be an all or none, black and white decision. There are numerous factors that impact the utility of multiplex respiratory pathogen panels. And the one item I didn't see mentioned in the LCD proposed is judicious patient-based ordering practices.

So if we go to the next slide, this is an example of test ordering algorithm that does include the respiratory pathogens panel that's in the box highlighted in red. This was actually one that we created for coronavirus during obviously the ongoing pandemic. It also included influenza and RSV concerns. And we do have the respiratory panel, PCR, nasopharynx in there as an option. It's really though under the panel or under the option where you have a patient with an influenza-like illness that has risk factors for complicated disease.

Now note that we also have other options if the patient doesn't have these risk factors and isn't undergoing testing for public health or work or travel reasons. We just say testing is not indicated. And many of our algorithms will go down these different aspects where we'll say that testing isn't indicated at all or maybe selective.

So if you go to the next slide, the other part of this is delivering the result in a timely manner. And in my mind, if you have a rapid test but you deliver the results within one to two days afterwards, then that really isn't providing a meaningful result. This is our turnaround time for the respiratory panel by FilmArray. Our mean turnaround time is 2.5 hours.

And you can notice from the different colors on the bottom that we perform this during the day shift to evening shift and the midnight shift. We do this as soon as they come in. They are prioritized.

There is some variability that somewhat shifts this. Sometimes we go up to four or five hours although that was really during two large peaks of COVID-19 where we

were just very hard hit with a lot of different tests at that point. But overall it actually is pretty steady with our turnaround time between two to three hours.

So next slide please. So I picked out a couple of examples from the literature that were cited in the proposed LCD. And I wanted to just comment on a couple of them. I actually think that there are several manuscripts in the literature with data that do support the use of a more than five pathogen respiratory panel.

But if we go to the next slide, I'm just going to comment on two that were actually mentioned in the LCD proposal itself. The first is by (Brittany Long), et al. in 2011. I thought this was a great study, randomized study to control - or to determine if multiplex testing would have an impact on antibiotic prescriptions which really is one of the important points here because we're in this global pandemic of antimicrobial resistance that is becoming widespread and will be very expensive. We need to be able to control that.

They looked at that. I think it's interesting. They had their patients randomly assigned to one of two groups, one which they called "Rapid." But as I highlighted in red, their rapid results were actually in 24 hours which to me is rather long. The delayed cohort for getting the results from testing was 8 to 12 days.

But even with that delayed 24-hour turnaround time, they still found that in that acute setting when patients first came in with symptom duration of less than or equal to five days that that group received fewer antibiotic prescriptions in - than patients in the delayed result.

So they - and it was statistically significant even with this, what I would consider to be, unacceptably long delay they still saw statistically significant difference.

Now the study goes on to say that at ten days when they looked at those two groups, there was no significant difference. To my mind though, that reflects patient follow-up practices and the physician response to symptomatic patients.

Presumably the patients that were initially not given antibiotics that didn't get better within the next day or two came back. And at that point the physician not knowing, you know, wanting to help the patient gave antibiotics. So to me, that really reflects the need for physician education and followup practices but doesn't reflect the utility of the test itself.

So if you go to the next slide, additional supportive data. There was also this other paper in 2018, a randomized non-blinded study. And this study actually did show positive results as well without any caveats. Patients were randomized to receive testing with the respiratory FilmArray Panel within two hours versus an IFA in 26 hours. And the patients in the FilmArray Respiratory Panel were associated with changes in medical management. That was also statistically significant.

So I - the authors had discussed that perhaps it would be hard to take some of these smaller studies and expand them to the larger population but yet we have several of these studies that do seem to show that medical management is changed with use of a respiratory pathogens panel of more than five (NLAs).

So next slide please.

So in summary, there are well-designed studies that have demonstrated a positive impact with multiplex respiratory panels with more than five (NLAs) and decreasing unnecessary antibiotic use or changes in patient management.

And so we would really argue that reimbursement must be considered in the context of the entire healthcare system. Using the available data, I think it's very challenging when you're talking about outpatients to use an all or none approach. These are patients that may be immunocompromised, that may be extremely ill, that may be hospitalized the very next day, that may have severe underlying respiratory disease and outpatients are such a diverse group. It really needs to have a good ordering algorithm in place to support it.

So judicious use for multiplex respiratory panels is an important component of preventing the emergence and spread of antimicrobial resistance. And I'll just say again that this is a significant and costly global issue. We have the power to influence this now with appropriate test utilization.

So with that, I will stop and I would love to answer any questions.

Dr. Ola Awodele: Thank you very much. And no, I don't have any questions. I would just want to say that these studies that you did point out rightfully so that also a big part of their conclusion was the importance of getting the turnaround which we have reflected in the policy, a quick turnaround and effective system in place to be able to deal with the results. But I do appreciate and thank you for your presentation.

Operator, could you please check if there's anybody who would like to make comments about this draft policy?

Coordinator: Absolutely. We would like to open the phone lines for any questions or comments. If you do have a question or comment, please use star 1 on your phone.

And one moment to see if we have any.

And I am currently showing no questions or comments. Thank you.

Dr. Ola Awodele: Thank you Operator. Dr. Duerden, over to you.

Dr.Duerden: Thank you. So the next policy we're going to be discussing is the epidural procedures that are used for pain management.

The first two slides are going to be dealing with the indications. I'll just preface that this - sorry, this policy was assessed and vetted with a multi-jurisdictional CAC on February the 11th, 2021 where we sought significant amount of input from the multiple societies that represent the physicians that do these epidural injections as well as the experts that were on the CAC panel.

For the policy we have the start of the first indication for an epidural would be that you can have an epidural injection would be considered necessary for the following three requirements.

And that is that they have to have a history in physical examination with concordant radiologic imaging could show the diagnosis that they're treating and it has to be supported by the findings of either a lumbar, cervical, thoracic radiculopathy or - and/or neurogenic claudication due to that central disc herniation, osteophyte - or osteophyte complexes that could occur, severe degenerative disc disease or producing foraminal or central spinal stenosis or post laminectomy syndrome or acute herpetic associated pain and is that they need to have radicular pain that is severe enough to cause a significant degree of functional disability or vocational disability based on an objective scale.

And I'm going to touch base with that on the third slide.

That functional scale must be performed at baseline if the function is to be considered as part of that assessment. And the epidural would be considered reasonable and necessary if the pain duration is for at least four weeks when there's an inability to tolerate noninvasive conservative management or medical documentation of failure to respond to four weeks of non-invasive conservative care or acute herpes zoster refractory to conservative management where four weeks of waiting is not required.

You can go to the next slide.

The additional indications for epidurals would be that they must be performed with CT or fluoroscopy, image guidance with contrast. They need to be - sorry, the transforaminal epidural injections need to involve a maximum of two levels at one spinal region. It's important to recognize that most conditions would not ordinarily require epidural injections at two levels in one spinal region.

Fourth, the caudal epidural injections and the interlaminar epidural steroid injections involving a maximum of one level are considered reasonable and necessary.

Five, it is reasonable and necessary to perform transforaminal epidural injections bilaterally when clinically indicated.

Six, a repeat epidural steroid injection when the first injection directly and significantly provided improvement of the condition being treated may be considered reasonable and necessary when the medical documents show at least 50% of sustained improvement of pain relief and/or improvement of function based on the scale that was used at the beginning - before the epidural injection was given.

Seven, that epidural injections must include corticosteroids, anesthetics, anti-inflammatories and/or contrast agents.

Eight, the epidural steroid should be performed in conjunction with conservative treatments.

Nine, the patient should be part of an active rehabilitation program, home exercise program or functional restoration program.

Go to next slide. This slide discusses the scales which can be used and they are not inclusive. So these are acceptable scales but not limited to the verbal rating scales, the numeric rating scale, the visual analog scale, the pain disability assessment scale, the Oswestry Disability Index, the Oswestry Low Back Pain Disability Questionnaire, the Quebec Back Pain Disability Scale, the Roland-Morris Pain Scale, the back pain functional scale or the patient-reported outcomes measurement information system scale.

These are to be - or can be used and/or would be considered reasonable scales or other scales that could be used. But they need to be used at the beginning and after the epidural injection has been performed.

Next slide. Like to deal with the policy's limitations on epidural injections. And that is epidural injections performed without image guidance or by ultrasound are not considered reasonable and necessary.

Two, epidural and steroid injections performed with biologics or other substances not FDA designated for this use are considered not reasonable and necessary.

Three, it is not considered reasonable and necessary to perform multiple blocks such as epidural steroid injections, sympathetic blocks, set blocks, trigger point injection during the same session as the epidural steroid injection with the exception of a (unintelligible) in an epidural steroid being performed in the same session.

Four, the use of general anesthesia, moderate sedation or monitored anesthetic care, is usually unnecessary or rarely indicated for those procedures and therefore not considered medically reasonable and necessary. In exceptional cases, documentation must clearly establish the need for sedation in this specific patient.

Five, epidural steroid injections used to treat nonspecific low back pain, axial spine pain, complex regional pain syndrome, widespread diffuse pain, pain from a neuropathy from other causes, cervicogenic headaches are considered investigational and therefore not considered medically reasonable and necessary.

And six, epidural steroid injections are limited to a maximum of four sessions per spinal region in a rolling 12-month period.

You can go to the next slide. I'll finish up with the limitations.

Seven, it is not considered medically reasonable and necessary for more than one spinal region to be injected in the same session.

Eight, it is not considered medically reasonable and necessary to perform transforaminal epidural injections at more than two nerve root levels during the same session.

It is not considered medically reasonable and necessary to perform caudal epidurals or interlaminar epidural injections at more than one level during the same session.

It is not considered reasonable and necessary to perform caudal epidural injections or interlaminar epidural injections bilaterally.

It is not considered reasonable and necessary to perform epidural injections in a series.

And then the next slide, I'll finish up the last few limitations. And that is number 12, steroid dosing should be the lowest effective amount and should not exceed 40 milligrams of methylprednisolone, 10 milligrams to 20 milligrams of triamcinolone acetate or 10 milligrams of dexamethasone phosphate per the session.

And 13 and finally, it would generally not be considered reasonable and necessary for treatment with epidural injections to extend beyond 12 months. Frequent continuation of epidural steroid injections over 12 months may trigger a focused medical review.

Usually on the 12th month requires the following: The pain has to be severe enough to cause a significant degree of functional disability or vocational disability. The epidural injection needs to provide at least 50% of sustained improvement of pain and/or 50% objective improvement in function using those scales that were tested at baseline.

The rationale for the continuation of epidural steroid injections including but are not limited to a patient is - who is a high surgical risk candidate and couldn't have surgery. So - or a patient that does not desire surgery or the patient that has recurrence of pain in the same location relieved with an epidural steroid injection for at least three months.

And the communication with the primary care provider regarding the patient's candidacy for prolonged repeat steroid epidural injection use.

So having outlined those continuation policy indications and limitations, I understand we have someone who would like to make a presentation. So I'll turn the time over to Dr. Rittenberg.

Dr. Rittenberg: Hi there. Are you able to hear me okay?

Dr. Duerden: Yes sir.

Dr. Rittenberg: Okay, great. Yes. Thanks for having me on to comment on this. I'm at Kaiser Permanente in California. I'm representing the Spine Intervention Society as well.

Go to the next slide. I have no disclosures. You can go to next slide.

So just a few comments on, you know, indications. And these are kind of minor ones. So with history of physical (unintelligible) radiculopathy or neurogenic claudication, you should probably (unintelligible) radicular pain rather than radiculopathy. You know, the distinguishing point is a radiculopathy is generally accompanied by neurologic deficits. So radicular pain is really the indication that we're treating. So many patients will have severe radicular pain without any, you know, physical examination findings of neurologic deficit.

Also commenting on straight leg raise, that is a specific test for radicular pain but it's not very sensitive. So a lot of times it will not be present. Most importantly patients with radicular pain who do not have a positive straight leg raise or neurologic deficit are just as likely to respond to epidurals as those who do have those findings.

Next slide. So we would suggest, you know, rewording that history and/or physical examination and diagnostic imaging supporting one of the following lumbar, cervical or thoracic radicular pain.

You can go to next slide. You know, and going to covered indications. For the requirement of four weeks pain duration, we do feel that it's unrealistic to expect a patient with acute radicular pain from a disc herniation to delay epidural steroid injection. These are actually the patients that kind of benefit the most from the procedure. So we'd suggest rewording as pain duration of at least four weeks with exception made for severe radicular pain where a four-week delay cannot be tolerated.

Next slide. Okay, next on requirements for the use of contrast. Again we fully support the use of contrast except in patients who have a documented contrast allergy or who are pregnant. So suggesting the following wording, you know, epidural steroid injections may be performed under CT or fluoroscopic guidance with contrast. And unless the patient has documented contrast allergy or is pregnant and then, you know, add that ultrasound guidance without contrast may be considered in these in similar circumstances.

Next slide. Again, covering indications, repeat injections if after an initial injection the patient's pain returns prior to three months, it is reasonable to attempt to reinstate relief with a repeat injection. If there's a three-month threshold required after initial injection, a significant number of patients who otherwise obtain relief from a second injection may proceed onto surgery.

Next slide. So we would suggest the following change in wording. Repeat ESIs are appropriate when one to two prior, you know, epidural steroid injections provided prolonged reduction in radicular pain of at least 50% relief and for at least three months for the condition being treated.

ESI should not be repeated within 14 days. If a patient fails to respond to a - well to a single ESI, a repeat ESI after 14 days can be performed using a different approach and/or different medication with the rationale and medical necessity for the second ESI documented in the medical record.

Next slide. You know, this is for ESI injections. So the current wording is somewhat confusing. So what we're saying is if the injections do not include steroid, then they are not epidural steroid injections. So I suggest replacing "ESI injectate" with "epidural injectate." So the wording that we would recommend is the epidural injectate must include contrast agent unless the patient has a contraindication to contrast. Injectate may also include corticosteroids, local anesthetic, saline and/or anti-inflammatories.

Next slide. The cover indications, so the requirement for other conservative treatment, while some patients will certainly benefit from multimodal treatment, there are others who experienced relief from an epidural steroid injection and may not require additional conservative treatment. So we suggest rewording to include - to indicate that epidural steroid injections may be performed in conjunction with conservative treatments.

Next slide. New indication diagnostic spinal nerve block. We suggest including "the following diagnostic spinal nerve blocks are performed by injecting anesthetics after a single spinal nerve to help confirm or rule out the source of the patient's pain often to assist in surgical planning." These blocks utilize the same CPT codes as transforaminal epidural steroid injections and should be allowed in patients that may have failed a therapeutic epidural steroid injection when the medical necessity is documented in the medical records.

Next slide. So also limitations. So I'm just going to - I have one extra slide in my set here. So I'm going to go a little differently here.

So under Number 6, the limit of four epidural steroid injections per 12 months would suggest considering allowance of three epidurals for six months and 6 for 12 months regardless of the number of levels involved.

And then going back to Number 1, which is, you know, injections performed without image guidance or by ultrasound guidance. So just allowing for ultrasound guidance for patients with documented contraindication to contrast media.

And then at Number 11, under series of epidural steroid injections, while we do not support a series of three, we do support repeat injections if previous injections were successful in achieving pain relief and functional improvement for only one - or if only - or only one prior injection was unsuccessful.

So we suggest rewording as follows: “It is not medically reasonable and necessary to prescribe a predetermined series of epidural steroid injections.”

Next slide. Steroid dose. If you look at doses that are recommended or inaccurate, data from studies looking at dosages implemented in transforaminal injections have been inappropriately extrapolated here to interlaminar injections.

So we suggest rewording (unintelligible) slightly higher dosages consistent with the previous version of the LCD. Steroid dosage should be the lowest effective amount, not to exceed 80 milligrams of triamcinolone or 80 milligrams of methylprednisolone, 12 milligrams of betamethasone or 15 milligrams of dexamethasone per session.

Number 13. Treatment exceeding 12 months, we feel that this limitation is unreasonable and the requirement to add a significant documentation burden to explain that a patient does not wish to proceed with surgery. We suggest omitting this. Requiring the patient to communicate with the primary care provider to discuss whether the patient is eligible for prolonged repeat steroid use places undue burden on physicians and should not be required.

Next slide. Provider qualifications. We’re recommending consider replacing “healthcare professionals” with “physicians.” The physicians have the requisite training to accurately select patients, safely perform technically demanding procedures and to immediately recognize, evaluate and address potentially serious life-altering complications.

Next slide. We recommend the following language: Patient safety and quality of care mandate that healthcare professionals who perform epidural injection procedures for

chronic pain, not surgical anesthesia, are appropriately trained by an accredited allopathic or osteopathic medical residency or fellowship program in an ABMS or ALA-accredited specialty whose core curriculum includes the performance of management of the procedures addressed in this policy.

If the practitioner works in a hospital at any time and/or is credentialed by a hospital for any procedure, the practitioner must be credentialed to perform the same procedure in the outpatient setting.

And the minimum training must cover and develop an understanding of anatomy and drug pharmacokinetic - pharmacodynamics and pharmacokinetics as well as proficiency in diagnosis and management of chronic pain related disease, the technical performance with the procedure and utilization of the required associated imaging modalities.

Next slide. (Unintelligible) another side as well. So in terms of society guidance which is part of this, it should be also noted that the North American Spine Society revised their coverage policy recommendations in 2020. And these should be reviewed and replaced with 2013 and 2011 references that were listed on Pages 25 and 26.

Also, there were some typos of the following society names to warn the American Society of Anesthesiologists, American Association of Neurological Surgeons and Congress of Neurological Surgeons and Spine Intervention Society.

Thank you very much and thanks for the opportunity to make this presentation. Any questions?

Dr. Duerden: We appreciate you. I don't have any questions but I appreciate your review and significant number of comments and absolutely we'll take this under advisement.

Dr. Rittenberg: That's great. Okay. All right, thanks very much.

Dr. Duerden: Thank you sir. Operator, can you check and see if there's any other comments about the draft policy?

Coordinator: Absolutely. Again that's star 1 if you have any questions or comments on the phone. One moment to see if we have any questions or comments.

Dr. Duerden: Hearing no additional comments, I'll go ahead and close the comments for this draft policy and turn the time over.

Dr. Ola Awodele: Right. Thank you, Dr. Duerden:

The next draft that we will be discussing is non-invasive fractional flow reserve, FFR, for stable ischemic heart disease. And this is a new draft. But just historically these procedures were described using T codes. And when the T codes first of all came out, NGS decided to include them in our CCT, CCTA policy.

And pending more literature to further help us make policy which we have now been able to receive - we've now received and now we're able to separate them out and create their own policy. They also have the T codes. They now have the Category 1 code.

So the indication in this draft policy they said, FDA approved FFR-CT technology may be considered reasonable and necessary in the management of patients with symptomatic stable ischemic heart disease when the CCTA analysis is completed and demonstrates one of the following criteria.

Number one, left main disease with intermediate coronary stenosis, lumen diameter reduction of 30% to 50% or proximal and mid-left anterior descending coronary artery disease with intermediate coronary stenosis that is lumen reduction 40% to 70% or proximal and mid-left circumflex disease with intermediate coronary stenosis that is a lumen reduction of 40% to 70% considered equivalent to two-vessel disease or proximal two- or three-vessel disease with intermediate coronary stenosis in at

least two vessels or right coronary disease with intermediate coronary stenosis that is lumen reduction 40% to 70%.

Next slide please. The limitations in this draft LCD. FFR-CT is not considered reasonable in the following clinical circumstances: Severe obesity, that is BMI greater than 39 kilograms per meter square; prior placement of prosthetic valve; non-severe aortic stenosis; prior placement of graft in coronary bypass surgery; suspicion of acute coronary syndrome, that is where MI or unstable angina have not been ruled out; intracoronary metallic stent that is post heart transplantation.

Next slide. And limitations continue. Risk in MI, that is 30 days or less; prior pacemaker or defibrillator lead placement; newly-diagnosed systolic heart failure with no prior left heart catheterization; left main coronary artery disease with intermediate coronary stenosis that is lumen reduction less than or equal to 30%; non-obstructive stenosis on CTA that is less than 50% of all major epicardial vessels or catheterization in the past 12 months in the absence of a new symptom complex.

Next slide please. This service should not - sorry, this service should be performed in patients with stable coronary symptoms, as the title infers. It should not be performed until after the base study -- that is CCTA -- has been completed and interpreted. If higher grade stenoses are present that is greater than 70%, this study is not medically necessary as the patient should proceed to catheterization.

Similarly, low grade stenoses do not require additional confirmatory data. That would be in the case of less than 30% stenosis.

If more than two intermediate risk coronary lesions are identified, the clinical situation is considered high risk and the patient should proceed directly to catheterization.

And the last slide. While FFR-CT shows an exciting potential for reducing the need for an invasive coronary angiogram, the precise role for its use has not yet been entirely determined. The review PPV of - positive predictive value of FFR-CT between 52% to 65% and the low correlation in the 0.7 to 0.8 lesion range of 46.1%

suggests the correlation between FFR-CT and invasive FFR in this group is 10% to 15%.

The role of FFR-CT and potential benefit in intermediate stenosis between 40% to 70% has been most clearly established. However, there is insufficient outcome data to define management changes based on FFR-CT for high grade that is greater than 70% lesion. That would typically triage to catheterization.

There is both limited evidence and a lack of major societal guidance on the use of FFR-CT and guide ischemic heart disease revascularization.

So we did have request to present or speak to this draft. And if Dr. Rogers is on the call, Operator, if we could open his line and I'll hand over to him.

Coordinator: Dr. Rogers, your line is open.

Dr. Rogers: Yes. Yes. Are you able to hear me?

Dr. Ola Awodele: Yes we can, Dr. Rogers. Please proceed.

Dr. Rogers: Thank you. Thank you for the opportunity to address this open meeting and of course all of our comments will be included in written comments as well. We can go to the next slide please.

The three areas I'd like to touch on each briefly are, one, an overview of the pathway just to clarify a couple of aspects. Second, to talk about exclusions as listed in the draft LCD and areas for potential suggested revision and then the same for the indications.

Go to the next slide please. The testing pathway is important to emphasize that the pathway as has been described begins with coronary CTA and that in the majority of patients that is the only test needed including patients who have very severe disease as well as patients who have minimal or no disease identified by the CTA. It is in the

middle portion, patients with some disease and we'll talk about the specific severity in a minute.

We'll then pass through the HeartFlow FFR-CT analysis. And his management is then guided cognizant of that information.

Move to the next slide please. In terms of the proposed exclusions highlighted on this slide are sticks that we will address specifically for suggested revision in the final LCD.

Next slide please. The first three of these six we will address as a group. These are the severe obesity BMI over 39, prior prosthetic heart valves and prior pacemaker and defibrillator leads.

Go to the next slide please. I like to emphasize that all of these relate to concerns about CTA image quality and whether or not image quality will be degraded to a degree that the HeartFlow FFR-CT analysis cannot be completed.

In terms of the process HeartFlow undertakes for providing FFR-CT doing FFR-CT analysis, that process begins very specifically with an assessment of coronary CTA image quality. As a quantitative assessment it is part of our FDA clearance this aspect of our process. Each vessel is reviewed and graded for image quality. Again there's a quantitative scoring method applied.

And for cases which fail to meet the sufficient image quality to process for FFR-CT, there is no analysis performed and there are no charges for the service in those cases.

Furthermore, we provide an explanation for each failed case as well as training to help improve image quality for future studies.

Go to the next slide please. This shows an example just for people to see visually what we're talking about, moving from excellent to satisfactory to poor image quality

and it's readily apparent even to a novice observer the level of fidelity that one sees in terms of the coronary lumen. The lumen in these pictures appears light. The contrast is light. And one can see of course in the poor image quality it's very hard to discriminate the borders of the arteries.

What we see overall is above 90% acceptance rate for real world users. But again there are cases which fail quality. Sometimes the failure is related to artifacts and pacemaker leads or prosthetic heart valves or patients who are - whose BMI is so high that it obscures adequate imaging but there are other patients who have those same conditions and whom the image quality is acceptable and we do provide the FFR-CT analysis.

Next slide. If you go to the next slide again please.

So our proposed revisions for these three exclusions is that the image quality - CTA image quality data is unacceptable that we provide feedback and there is no processing and no charge. So we suggest that these exclusions be removed from the final LCD.

Next slide. The next two I'd like to address are known severe aortic stenosis and suspicion of acute coronary syndrome. The first, known aortic stenosis, part of the FFR-CT analysis process considers what aortic stenosis does to the heart which is to cause hypertrophy of the left ventricle and increase left ventricular mass. These changes are measured on CTA as part of our process and we take them into account in doing the FFR-CT analysis.

There is no reason to suspect different physiology other than that effective hypertrophy. And therefore the calculations that go into the FFR-CT analysis should be consistent and accurate in aortic stenosis. So we suggest removing this.

The second, suspicion of acute coronary syndrome, first is suggestion that this wording be revised to mirror what was revised and incorporated in the final LCDs from Palmetto, Noridian, CGS and WPS. That language is shown on the slide and it

is that suspicion of acute coronary syndrome where acute MI and unstable angina have not been ruled out is the exclusion. That means that patients who may have suspicion of acute coronary syndrome but in fact don't have acute coronary syndrome but have stable chest pains and be included as covered in the final LCD.

Next slide. And then the final draft exclusion we suggest modifying is intracoronary metallic stent HeartFlow is indicated for and labeled for some patients who have intracoronary metallic stents. The list of those is shown below, the list of patients for whom we are not indicated and is not within our IFU. It is a subset of patients who have intracoronary metallic stents and we would suggest that the final LCD reflect what is in our product labeling.

Next slide. In terms of the list of proposed inclusions, we won't review them. They're captured here as they were read by the prior speaker.

Next slide please. And I want to highlight the group of patients and the stenoses which are above the current suggested proposed LCD boundaries of 40% to 70%. That is patients in whom the stenosis is 70% to 90%. There is substantial published outcomes data related to utility and outcomes in this set of patients. If one looks in this table in the box to the right, patients whose stenosis is 70% to 90%, have a negative FFR-CT analysis. In other words, they may well not need to go to the cath lab if that stenosis is in the LAD at 17% of patients.

If it's in the left circumflex, nearly 40% of such patients will have a negative FFR-CT and potentially avoid a trip to the cath lab even though their stenosis is 70% to 90%. And for the RCA it's nearly 1/3 of patients.

So the utility in this group of patients is significant and a significant proportion may be able to be managed conservatively, avoiding the risk and expense of invasive angiography even though they have a stenosis over 70%.

Next slide. In terms of data from our studies and the reference, I apologize, is on this slide. The formatting has made it hard to see. It's from our advanced registry which

suggests - and this is for the utility in these patients that 62% of patients in a 5000-patient prospective registry with clinical follow-up published out to one year that 62% of these patients had a different management plan after the physicians were provided with the FFR-CT than they would have after the CTA alone.

So the notion is the data are strong and it's quite clear to current users that patients who have a 70% to 90% stenosis have a substantial amount to gain from having access to FFR-CT when their physician thinks that may be of help in their management.

Next slide. So in terms of proposed revision to the list of inclusions, it is our suggestion that this - the left main, number one, remain just as it is but that the others be revised to coronary artery disease with coronary stenosis of uncertain functional significance and a lumen reduction of 40% to 90% rather than 40% to 70%.

Next slide. Thank you very much for the opportunity and certainly would be happy to address any questions which may be - which people may have at this time.

Dr. Ola Awodele: Thank you, Dr. (Rogers). I don't - thank you very much for presenting these findings and I don't have any follow-up questions. But as you had said, thank you for also saying that - mentioning that you will be sending them in writing which I do appreciate you bringing that up because I haven't really mentioned it to the other people who are - who have presented today. So if they could please send the presentations and all comments in - to us in writing, we would appreciate that.

So is Dr. Marshall on the call? Operator, if he is, if you could please open up his line. I believe he has comments.

Coordinator: Dr. Marshall, your line is open.

Dr. Jeff Marshall: Hello? Hi. Well, thank you for allowing me to speak. My name is Jeff Marshall. And I guess first, can you hear me?

Dr. Ola Awodele: Yes we can, Dr. Marshall. Please proceed.

Dr. Jeff Marshall: Okay. So like I said, I'm a board certified interventional cardiologist. And I have no conflicts of interest and I'm not receiving any financial support for this.

I'm here today actually representing the Society for Cardiovascular Angiography and Interventions, abbreviated SCAI. And SCAI is the largest, not-for-profit professional association of interventional cardiologists with almost 5000 members.

SCAI promotes excellence in interventional cardiovascular medicine through education, representation and advancement of quality standards to enhance patient care.

SCAI believes that there's strong scientific evidence for performance of FFR-CT as a non-invasive diagnostic test in patients with stable ischemic heart disease and intermediate coronary artery disease by CTA.

SCAI is specifically pleased that the proposal of the local coverage decision does not place restrictions on coverage of invasive FFR which is a complementary procedure to FFR-CT.

Invasive FFR is performed at the time of a coronary angiogram to evaluate specific lesions or blockages within the coronary arteries. And generally speaking interventional cardiologists, while they're actually performing an angiogram, use invasive FFR as a physiologic test to determine whether or not to perform or defer percutaneous interventions. That is to do angioplasty, replace a stent.

Indeed, in some situations, the performance of invasive FFR at the time of an angiogram report - results in the avoidance of unnecessary coronary interventions and that reduces cost.

There are, however, significant differences in the accuracies of invasive FFR and FFR-CT. And like I stated before, several studies have shown that in some cases, FFR-CT positive lesions end up having negative invasive FFR procedures and interventions are deferred or avoided. FFR is a very sensitive test and interventional cardiologists use it. By default, there are a number of false positives that can be either confirmed or refuted with invasive FFR if the patient indeed goes on to angiography.

Invasive FFR does remain the gold standard for assessing complex coronary disease and invasive angiography. And I think it's still the best way to accurately assess serial coronary lesions. And an invasive FFR is accompanied like FFR-CT by lots of outcomes data from large numbers of clinically randomized trials.

So as an interventional cardiologist, I'm not here to review the details or restrictions of the coverage for FFR-CT that are contained in your current proposal. We actually defer to the experts that have spoken or will speak on those matters.

So in summary, SCAI supports NGS's proposal to codify coverage for FFR-CT and are pleased the proposal does not restrict subsequent coverage of invasive FFR procedures.

In the future, if NGS identifies individuals that are routinely that is on every case doing both FFR-CT and invasive FFR, we believe that that should be investigated. FFR-CT is complementary to invasive FFR physiology and not a substitute.

And I'd like to thank Dr. Cigarroa and (unintelligible) who put this together. And as a professional society, we like to offer to the national government services that as it continues to review this proposed LCD, please don't hesitate to contact Mr. Wayne Powell, part of our advocacy group, and his phone number is 703-772-7910 and his e-mail address is wpowell, p-o-w-e-l-l, at-scai, S-C-A-I, dot-org.

Thank you very much for having me today.

Dr. .Ola Awodele: Thank you, Dr. Marshall. Again if you could please put those comments in writing and send them to us, we would appreciate that.

Dr. Jeff Marshall: I will do that.

Dr. Ola Awodele: Operator, could you please check - thank you very much, Dr. Marshall. Operator, could you please check if anybody on the line - anyone else on the line has comments?

Dr. Boren: Dr. Awodele, Dr. Boren, Can you hear me?

Dr. Ola Awodele: Yes I can.

Dr. Boren: A question for Dr. Marshall and a statement for Dr. Rogers. For Dr. Marshall, what percentage of the time do you think they should be getting the FFR with their coronary computed tomography? I mean, is this something you expect, you know, 5%, 100%, any ballpark figure?

Dr. Jeff Marshall: Can you hear me?

Dr. Boren: Yes sir.

Dr. Jeff Marshall: Okay. I don't have specifically a ballpark figure. I think that these are instantaneous decisions made by an interventionalist when they see the anatomy. We use FFR-CT a lot and we can see the anatomy there. But I have to say that is interventional doctors are much more used to interpreting angiograms. And when we see intermediate lesions, we want to then confirm or refute that to avoid putting in unnecessary stents.

So I can't personally give you an absolute number. I think that the number is low only because my personal experience with my non-invasive partner sending FFR-CT to me that it seems to be quite accurate. It is a very sensitive test. So the number of

false positives are real and that's what we can confirm or refute in the cath lab. Sorry, I don't have a specific number.

Dr. Boren: Okay. So, in the cath lab, - percentage-wise, do you have any guess what percentage of patientsin the cath lab get?

Dr. Jeff Marshall: Well, that varies from cath lab to cath lab. And this is just how physicians are trained and what they understand about the difference between anatomy and physiology. In some laboratories, invasive FFR is used in almost every intermediate lesion. In some cath labs, anatomy is used more often.

But the national use of invasive FFR is creeping up. I don't know the most recent numbers but I would say that it's less than 10% or 15% of all patients that undergo coronary angiography that receive invasive FFR. But that number has been creeping up over the last five to ten years.

Dr. Boren: Okay. Okay. Thank you. And for Dr. (Rogers), one point we need to make is that, you know, you state that your company, if it's a poorly qualified - poor quality study, you don't charge for it and therefore we don't have to worry about a number of these exclusions. But you must understand that this policy has - is not specific to any proprietary product.

And while your company obviously is very - has a lot of integrity, it's quite possible that other companies might not be as magnanimous as your company and they might continue to build for poor quality services. So again, this is not a product-specific LCD. It is a, I hate to say, generic but that's probably the best. Thank you very much.

Dr. Ola Awodele: Thank you, Dr. Boren. So, Operator, could you please ask people on the line if they have any additional comments concerning that draft policy?

Coordinator: Yes, absolutely. Yes, absolutely. If you do have any questions or comments, please use star 1. It looks like we do have Irfan Zeb from WVU Institute. Your line is open.

Dr.Irfan Zeb: Hi. Can you guys hear me?

Dr. Ola Awodele: Yes we can. Please proceed. Thank you.

Dr. Irfan Zeb: So I'm a non-invasive cardiologist from West Virginia. And I'm also a member of Society of Cardiovascular Computed Tomography that deals with coronary CT angiography.

So I agree with the comments made by Dr. (Campbell) and I don't have any comments at this time. However, we will also submit our comments in writing to the NGS. Thank you.

Dr. (Ola Awodele): Thank you very much, Doctor. Operator, could you check if there's anyone else?

Coordinator: I am currently showing no one else in queue.

Dr. (Ola Awodele): Okay. Thank you very much. So I will proceed to the last draft. Yes. It was on the agenda for today. And it is actually concerning the cardiac computed tomography. That's the CCT. And coronary computed tomography angiography, the CCTA, policies that we currently have and it's a revision to those policies.

And basically in light of what we - the draft that we just discussed, the following indication has been deleted.

Letter J, FFR-CT, this test may be considered medically necessary when CCTA shows the idea of a certain functional significance or is non-diagnostic and where the addition of functional information provided by FFR-CT can help the physician determine which patient may require invasive evaluation and/or treatment.

And obviously I'd also say please refer to the new non-invasive fractional flow reserve, FFR, for stable ischemic heart disease which is currently in draft. So we do need to take these two policies through the same procedure so that when the other

one finalizes, this one can also be revised to show that so that there's no confusion and direction.

So I will hand over to - well, I think I can just let everybody know who's on the call that the official comment period - if you can go to the next slide please. Official comment period ends on July 17, 2021. We'd like to thank everybody who presented today and who had comments and also just remind everyone to please send information, send their comments in writing.

So anybody who wants to comment on a proposed LCD that we discussed today during the official comment period that is prior to July 17, 2021 should please send their comments to partblcdcomments@anthem.com and if I snail mail to National Government Services, Inc. LCD comments, PO Box 7108 Indianapolis, Indiana 462077108.

Thank you very much everybody and have…

Dr. Craig Haug: Dr.Awodele?

Dr. Ola Awodele: Yes, Dr. Haug?

Dr. Craig Haug: Yes, yes. Just to emphasize also, they send in those comments to include their conflict of interest disclosure. That's very important.

Dr. Ola Awodele): Okay. Yes, sorry. Please do include your conflict of interest. I believe we're done for today. Operator, you may disconnect the call.

Coordinator: Thank you all for participating in today's conference. You may disconnect your line and enjoy the rest of your day.

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