ANTHEM, INC.
Moderator: Susan Bentz
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OPERATOR: This is Conference #6389895.

Operator: Ladies and gentlemen, thank you for standing by, and welcome to the NGS J6 and JK Opening Meeting.

At this time, all lines have been placed in a listen-only mode. After the speakers' presentation, there will be a question-and-answer session. To ask a question during the session, you will need to press star one on your telephone. Please be advised that today's call is being recorded. If you require any further assistance, please press star zero.

I would now like to hand the conference over to your speaker today, Carolyn Cunningham. Thank you. Please go ahead.

Carolyn Cunningham: Thank you, (Felicia). Welcome, everybody, that's here in person and also everyone that's on the phone. We had a little bit of delay, and we have a full agenda. So we'll sort of march right on.

(Felicia) – I mean, (Nikita), can we go to the next slide. Dr. Awodele is here, Dr. Boren is on the phone. Dr. Duerden is here, and Craig Haug is here. We don't have Dr. McKinney enlisted, but he's here with us here, too.

Craig, do you have anything you want to say?

Craig Haug: My name is not on there on purpose. So (inaudible). No, but welcome, everyone. Just a few technical things, if you're a speaker, we're going to ask you to come to the podium. There is a spider or an octopus or tentacle, whatever term you want, mike at the podium, and then your slides will be projected. So if you'll come to the podium, then the phone participants can hear you actually fairly well.

I want to welcome you again. As you know, this year has been sort of a change for us for the LCD development process. It's been a year of learning. CMS has changed the direction that we'd go in for developing our LCD. So I think we've acclimated well. We'll see what next year holds.

And without further ado, we'll turn it back to Carolyn for us to get rolling on her topics for today. So thank you for your attendance.

Carolyn Cunningham: Thanks, Craig. OK, Steve, we're glad you were able to join us. Let's start off with the first policy, Select Minimally Invasive GERD Procedures.

Craig Haug: Operator, could you open up Steve Boren's line, please?

Operator: I'm not showing his line connected at this – yes, it's connected. His line is open.

Craig Haug: OK. Steve, go ahead.

Stephen Boren: Can you hear me?

Craig Haug: Yes.

Carolyn Cunningham: Yes, we can. Can you hear in the back?

Female: Yes.

Carolyn Cunningham: OK, we're ready, Steve.

Female: Now, we can't hear you.

Carolyn Cunningham: Operator, we're not hearing, Dr. Boren.

Operator: His line is open (now). He may have muted on his end.

Stephen Boren: OK – let me just get a little closer to the screen. OK, the first one is the Select Minimum Invasive GERD Procedure, DL35080. This is really a reconsideration of the current policy that is under the new CMS regulations. We have to treat this like a new policy.

So we do have some presentations, correct?

Carolyn Cunningham: We do.

Stephen Boren: OK. We have the first one, please.

Carolyn Cunningham: You're talking about slides.

Stephen Boren: Yes.

Carolyn Cunningham: OK.

(Inaudible)

Stephen Boren: OK, here we go. And this is, in particular, we're talking about LINX and the Reflux Management System that people can read, and clinical data from the various studies are emerging. At this time, open label studies of patient registries with short-term follow-ups are the dominant source of data. The overwhelming preponderance of reviewers remained equivocal of this support and have called for randomized control trials for the clinical follow-up, long-term follow-up. And in the absence of such studies and the absence of wide acceptance, endoscopic treatments triggered in this case are not proven effective. This is not really a true – it's different than these other ones, but it's not proven effective.

And we have the analysis of the evidence and the number of papers. And we saw the SAGES Technical and Value Assessment Committee's (sic – Technology and Value Assessment Committee) paper, which we know is the – this is the lowest form of evidence. And in summary, there were concerns about the quality of evidence, including randomization, the above-mentioned likely patient overlap increased studies, and the concern of long-term efficacy and safety. Thus, a submitted medical evidence does not support a level to support the change of this contract, (its) non-coverage policy.

Carolyn Cunningham: Thank you, Steve.

Stephen Boren: You're welcome.

Carolyn Cunningham: Dr. (Noel is) coming to the front so you can have a microphone.

(Noel): Thanks.

(Inaudible)

(Noel): OK, great. Can everybody hear me OK? All right, thank you. I'll try and keep this to my 10 minutes or less.

Thank you for allowing me to speak with you all today about magnetic sphincter augmentation therapy. I'm a surgeon from Wisconsin at the Medical College, and I'd like to share with you a little bit of information about why I'm passionate that we should be able to offer this to our Medicare beneficiaries.

Next slide, please. So, who gets reflux? It turns out that Medicare beneficiaries get it just like a lot of other folks. GERD is a really common condition as everybody knows. Twenty percent of the United States population has reflux. Hospitalizations related for this condition have increased dramatically in the last few years, more than 200 percent over an eight-year interval. We know that the incidence of reflux increases rapidly as people age. In fact, in 2004, more than a quarter of Medicare beneficiaries were using GERD medications, and this accounted for more than or nearly $6 billion at the time.

Next slide, please. So reflux disease is inherently a mechanical disease. And so, the physiology is that lower esophageal sphincters fails in this condition. And the lower esophageal sphincter either becomes too weak, too short, or not enough of it remains in the abdominal cavity. It may migrate above the hiatus into the chest which is a hiatal hernia.

And in this context, with any of these three or a combination of these three factors that lead to the sphincter failing in a patient after they eat, when they bend over, when they strain, these two variables can combine to overcome the sphincter and lead to abnormal reflux of acid, digestive enzymes, and bile. And this is an important point. We have medical therapy for the acid component of it. We don't have a treatment for the rest of what reflux is.

If you could forward to the next slide. And so there's a critical need for a treatment for reflux disease that functions differently than medical therapy, which is our main stage first line treatment. So we have 21 million patients in this country on proton-pump inhibitors. And we know that up to 40 percent of these patients are still having symptoms that persist or breakthrough medical therapy.

We know that medical therapy does not stop reflux because of what I shared before. This is a mechanical problem. It's a failure of the sphincter. And so these patients who are on acid reduction therapy continued to have reflux. By having them take these medications, we've changed the character of reflux so it's less acidic but reflux continues to the same degree. So there's digestive enzymes, bile, recently ingested food in the reflux state. We're really not addressing the root cause of the problem with medical therapy.

Next slide. So the Nissen fundoplication is a current treatment option. It's been around for a long-time. The goal of a Nissen is to improve the sphincter function in a patient whose sphincter has failed. It's a reconstruction. You completely take apart the anatomy. You wrap the fundus of the stomach around the esophagus. You're doing a permanent procedure. You're using the fundus to do this reconstruction.

The fact of the matter is that there's a ton of variation and technique. There is not a standardized technique for the Nissen fundoplication. Everybody does it differently. I'm a foregut surgeon, my practice is almost 100 percent focused on GERD. A massive portion of my practice is fixing failed fundoplications.

I always get the (app) notes and review them and no one has ever done a fundoplication like the person before them. There's tons of variability, (displays) of tons of variability and outcomes.

We know that the fundoplication can lead to gas bloat, inability to belch, difficulty vomiting, difficulty swallowing. We also know that less than 1 percent of patients who would otherwise qualify for antireflux surgery actually choose to pursue it because this is the most commonly offered option.

Next slide. The Nissen fundoplication fails, as many as 15 percent of patients who have this and ultimately undergo a re-operation, and the cumulative failure rate is about one out of four. We know from the pattern of failure that about two-thirds of the failures that occur happened in the first two years. We're just not seeing the same pattern or timing or rate of failure with a magnetic sphincter augmentation device that we see with the Nissen.

Next slide. So the LINX Reflux Management System, this is – it augments the lower esophageal sphincter with this device that's implanted. It preserves the ability to

belch and vomit while reducing regurgitation system symptoms. The magnetic beads attract each other. And it precisely augments the lower esophageal sphincter that has failed.

So there's two parts to the procedure. One is re-establishing that junction between the esophagus and the stomach back into the abdominal cavity, so reducing a hiatal hernia; and then augmenting the pressure of the sphincter. And when I say it precisely augments the sphincters, I mean that because the magnets attract each other at a pressure that's equivalent to the force of a normal lower esophageal sphincter. So this is a much more physiologically reconstruction of that valve than a Nissen is.

The Nissen is a super valve, and that's where these symptoms come from. It's a super physiologic reconstruction and the length is much more physiologic.

Next slide, please. So a couple fallacies and unfair comparisons that have been out there. The LINX is not a lap-band, all right. It's fundamentally different. The lap-band is an obesity procedure. The band is placed around the stomach so there are acid-producing parietal cells above the band. The band is high pressure. It's intended to be high pressure, and it's intended to lead to satiety and restriction for the patient. You can see the band on the left in comparison to the magnetic sphincter augmentation device.

Lap-bands have gone in and more often come out now. There's a lot of failures with these. These are weight loss failures. It's a fundamentally different operation, and it's not a fair comparison.

The Angelchik is a reflux device that was used decades ago. You can see the Angelchik on the right. It's a very big device. It's a very heavy piece of silicone. The Angelchik actually worked for reflux, the problem is that it would migrate. And this is a much smaller profile, and we do not see migrations following the LINX like we did for the Angelchik.

Next slide, please. There have been quite a few studies published in the literature. There have been two randomized controlled trials, three Meta analyses, 14 single-arm studies, eight comparative studies published on magnetic sphincter augmentation. You can see the timeline.

Next slide, please. Magnetic sphincter augmentation has been established to be safe. There's more than 16,000 devices that have been planted worldwide, and you can see the follow-up on thousands of patients, where we see that the X plant rate is in the neighborhood of 2 to 3 percent. The erosion rate is very low at a fraction of a percent, about 0.1 percent, and there have been no mortalities attributed to the LINX itself.

Next slide, please. When we talk about erosion specifically, we know that erosions happen early; and, again, this is data for more than 16,000 patients. Most of the erosions occur between one and four years, at an average of about two and a half years. Erosions happened gradually and they're easily handled with either completely endoscopic removal of the device or a combination of laparoscopy and endoscopy. These are not sick patients. This can be done on a scheduled basis.

Next slide, please. We know that the magnetic sphincter augmentation is (inaudible) durable. There's five-year data looking at the LINX. There's published data. We know that patients have durable relief of their heartburn and their regurgitation. We know that they're able to stay off of their proton-pump inhibitors, and we know that they're satisfied at five years and beyond. We have physiologic data to support that (pH) studies at these intervals. We have better data on the magnetic sphincter augmentation device than we do on the current standard which is Nissen fundoplication.

Next slide, please. Some Medicare specific data.

Next slide. There aren’t a lot of studies conducted specifically in Medicare cohorts, but this is from the New England Journal article that was published as part of the pre-market study. We know that patients that were 65 years and older in this cohort, they preserve their ability to belch. Next slide. They preserve their ability to vomit just like other patients in the study, and they experienced the same symptomatic outcomes, the same improvement in their quality of life.

Next slide. This is from a randomized controlled trials showing that regurgitation is addressed by a magnetic sphincter augmentation device significantly, more effectively than we see with proton-pump inhibitor therapy. This is a randomized controlled trial comparing PPIs at a double dose to magnetic sphincter augmentation.

Next slide, please. With one-year follow-up. A randomized trial of the magnetic sphincter augmentation device versus the Nissen is not feasible. The Nissen fundoplication is a non-reversible surgical procedure. The fundus is not spared with a significant procedure or we do a reconstruction. It will be difficult to randomize patients.

Patients don't want Nissen fundoplication. Less than 1 percent of patients who would benefit from it are willing to do it. We don't believe that clinical equipoise is possible in a study like that. As I mentioned earlier, there's a ton of variability in Nissen fundoplication. It is as much art as it is science, and deciding what the optimal technique and standardizing that is difficult.

There are two studies out there that use propensity scoring techniques to compare Nissen versus LINX. Next slide. And in these studies, which included 114 and 50 patients, we know when we compare LINX to Nissen that improvement (through) HRQoL scores happened, and that the side effect profile was very different. So patients who had MSA had less difficulty dosing and less vomiting than following this, and then they experience similar improvements in GERD-related quality of life. We know that they have less regurgitation in other comparative studies, if they stay in hospital for a shorter length of time, and they're able to stay off of their PPI long-term.

Next slide, please. So in summary, I believe that the data supports the fact that MSA is safe, effective, and durable. The side effect profile compares very favorably to a fundoplication. I see this in my practice, I would much rather place a magnetic sphincter augmentation device in a patient or have one. A lot of surgeons who have reflux ultimately opt for the LINX as opposed to a fundoplication. It is a simple procedure. It can be standardized. I think this is an important option for our patients on long-term proton-pump inhibitors who have complications or persistent symptoms related to reflux on these medical therapies.

Less than 1 percent of candidates opt for surgery due to limitations as I described. And for those 30 to 40 percent of patients with poorly controlled reflux on proton-pump inhibitors, these results in a really high health care utilization and long-term health consequences. Our patients are kicking the can down the road, not willing to having this and they want something else. This is something that can fill the gap.

I have a list of patients with reflux disease who have Medicare who are just waiting for this to be an option for them. And they're informed patients. One of my patients on my list is a gastroenterologist himself. One of my patients is married to a gastroenterologist. I would like to be able to offer them what I consider to be a better option. And I think we need to be able to offer this to our Medicare beneficiaries in Wisconsin and beyond, so.

Carolyn Cunningham: Thank you. Thank you, Dr. (Gould). Questions or comments for Dr. (Gould) here in the room, on the phone?

Operator: As a reminder, to ask a question, you would need to press star one on your telephone. To withdraw your question, press the pound key. Please stand by while we compile the Q&A roster.

There are no questions at this time.

Carolyn Cunningham: Thank you, (Felicia). Thank you, Dr. (Gould).

(Jon Gould): Thank you.

Carolyn Cunningham: Next, we have Dr. Kahrilas from Northwestern. He's here and needs to go to clinic soon, right?

Peter Kahrilas: Good afternoon.

Carolyn Cunningham: Good afternoon.

Peter Kahrilas: Is there any way I can advance the slides?

Carolyn Cunningham: No, because we're – it's nothing here, sorry.

Peter Kahrilas: Could you bring my slides up? Could you bring my slides up, please?

Carolyn Cunningham: (Nikita), we need to go to the next presentation.

(Nikita): Yes, I'm trying, one moment.

Peter Kahrilas: So good afternoon. I'm a gastroenterologist not a surgeon. I worked at Northwestern for a long time. And I've had a peculiar interest in reflux disease for most of that time.

Slide. So, just to advance through this to the bottom, and these are medical data on treating reflux disease with proton-pump inhibitors. They made their reputation on healing esophagitis. And you can see there, the number needed to treat is very small to see here. But when you get the symptoms, it gets less and less effective, and the last they add here is regurgitation.

Go ahead and put that in, please. When it gets to regurgitation, the efficacy of proton-pump inhibitors is poor because what they do is they take the acid out, they don't stop reflux.

Slide. And advance that one more. So if you look at real indications for non-medical treatment, it's (these). And high on the list is regurgitation dominant reflux disease. The others are less important for today's argument. But the problem of esophagitis was solved with the PPI, its persistent symptoms that we deal with now.

Slide. Dr. (Gould) just went over this operation. This is the standard. So this is what now gets offered to people who need non-medical treatment. It's a Nissen fundoplication. There is a lot of variability. It's a complicated operation, and it is prone to problems.

Slide. We talked about randomized control trials. This is the randomized control trial for fundoplication. One, published not that long ago in 2011, now the primary outcome here, we're healing esophagitis and resolving heartburn. A secondary outcome was acid regurgitation, and you can see that there is some improvement in acid regurgitation for fundoplication versus the (comparator) which was esomeprazole in this trial. So, yes, surgical therapies are more effective for regurgitation.

Slide. But they have side effects. Dysphagia would be one. And here you can see the comparison between the PPI group and the fundoplication in post-operative dysphagia.

Slide. Even more impressive is gas bloat or inability to belch, inability to vomit. All of these things is very clear separation because of the fact that (Gould) pointed out, this is an overcompensation for a defective sphincter so it limits the outflow from the stomach even when it is desirable.

Slide. The reason for that is because the stomach not only you have a super competent valve, but it loses its ability to accommodate. Normally, when you eat, the stomach gets bigger. When you take the fundoplication and tie it in a knot, tie a knot around the esophagus you take away the fundus, you potentially damage the vagus nerve, and you lose the ability to accommodate. So you get these dyspeptic symptoms.

Slide. And just to go all the way through this. This is a study from Mayo Jacksonville looking at it, in-house group of fundoplication patients – there's another side to that, go ahead – pre-operative and post-operative and focus on the big 73 percent pre-operative, no bowel dysfunction. And what happens to them after the fundoplication? Diarrhea, bloating, abdominal pain, constipation, half of them became IBS patients basically.

Slide. Slide, please. I know this is a good one, but slide, please. And then there is the issue of more serious outcomes from fundoplication. These are studies, population-based studies, that looked at the long-term outcome and complications from fundoplication. Here's one that gets everybody's attention (there). And in the U.S. cohorts, so this is like the VA, a Washington database, all of that, death rates from fundoplication, 0.8 percent, 0.4 percent, 0.8 percent, that's pushing 1 percent.

Next slide. And then there are life-threatening complications in the same cohorts, 2 percent, 3.4 percent, 2 percent. This is not a benign operation, its real surgery. And you have real adverse events here.

Slide. So the problems with fundoplication are these, complications, breakdown, and secondary symptoms.

Slide. These are a list of procedural treatments for GERD that have been proposed and developed to some degree since we're going to focus on the LINX.

Slide. This is what it looks like. Intraoperatively, it's this little necklace of magnetic beads placed around the gastroesophageal junction.

Slide. And this was the first significant publication showing its efficacy. This was published in the New England Journal of Medicine. It was a 100-patient series, there

was no control. So it was not a randomized control trial, but they had a physiological outcome which was the control of acid reflux.

Slide. And there it is. So that's the control of acid reflux. At one year, you went from 10.9 percent esophageal acid exposure to 3.3 percent. Normal is anything under about 5 percent. So you basically normalized acid exposure time in the esophagus.

Slide. You saw this already, but it's a five-year outcome of that same cohort of patients focused on the regurgitation, which is the red line. It goes down like a stone and it stays down for five years.

Slide. This is a trial comparing magnetic sphincter augmentation to double dosed proton-pump inhibitors. So patients had failed single-dosed PPI, and you have the options of either doing something else with this MSA or doubling a dose of PPI which is common practice.

Slide. And this is the outcome of that trial in terms of eliminating severe regurgitation, 90 percent on one side and 10 percent on the other side.

Slide. And looking at the breakdown in regurgitation, here you can see a very profound difference between the MSA on the left and the twice daily PPI on the right. You basically get rid of regurgitation in 80 percent and reduce it into the rest.

Slide. Other outcomes, improve quality of life, satisfaction with current condition, equally discrepant between the two groups. So there weren't any adverse side effects coming in that were compromising quality of life.

Slide. You saw this data on safety. But in terms of explants, you're looking at about 2 to 4 percent of device removal, and this was from (total X). So this was overall about a 4,000-implant experience. When you remove the LINX device, you remove the LINX device, and the person is the same as they were before. It's not like a fundoplication where subsequent operations introduce yet more morbidity.

Slide. So if I were to look at this, you can advance one here. In terms of the attributes of the MSA device, it's conceptually valid; pretty obvious what it does. There's a physiological proof of principle. There's demonstrated symptom reduction both in controlled and uncontrolled trials. It has demonstrated pH control of both in controlled and uncontrolled trials. The safety data is acceptable. The only thing – wide

acceptance depends upon at this point is third party reimbursements. And I would advocate for that.

I think that's the end (of the slide). Yes. Thank you.

Carolyn Cunningham: Thank you. Questions or comments?

Stephen Boren: Dr. Boren here. I didn't see in any of your slides any conflict of interest statements.

Peter Kahrilas: Sorry for omitting it, but I don't have any.

Stephen Boren: Thank you.

Carolyn Cunningham: Any other questions or comments?

Operator: As a reminder, to ask a question, you will need to press star one on your telephone. To withdraw your question, press the pound key.

Carolyn Cunningham: Thank you.

Peter Kahrilas: Thank you.

Carolyn Cunningham: Dr. (Maish)?

(Mary Maish): Thank you for letting me speak today. I'm a thoracic and foregut surgeon in the Northwestern system. And I specifically trained with one of the individuals who masterminded this device. And there is no way that this device would have come as far as it had if it hadn't been scientifically found. Many of the people involved in this device, the creation of this device, are super aggressive scientists not just clinicians. And although I'm not a scientist anymore, I'm just a clinician, I can speak from the clinical side of things. And that's what I intend to do today. I will present a little bit more of the science, but many of my colleagues have already done that.

There are two couple things I want to say before I take a look at my slides. The first thing is with respect to the comments that were made in the first part of this talk today, and that is this is not something that is emerging. This is something that has been now around, and the data is supporting not just emerging the support of. And I implore you to take a look at the data closely to convince yourselves of the same thing that the science is now here to support what we want to do.

The second thing is this is not an endoscopic procedure, this is a laparoscopic procedure. So it is clinically the same as doing a laparoscopic Nissen fundoplication in terms of the approach, the surgical approach. From that standpoint, it is something that's done by surgeons not by gastroenterologist who are here supporting our efforts today.

Lastly, it has already been adopted by Medicare organizations in other parts of the United States. So in those areas, we have Medicare patients that already can be offered more than just the singular Nissen fundoplication that these Medicare patients who are paying the same dollar-per-dollar (move) are not currently being offered support for this device. So I think it's something that needs to be overturned and supported in our region.

The summary of the evidence for the MSA is, again, it's already here and it's not something that I think we need to continue to nitpick at the early beginnings. We're going to continue to study it obviously. But already, we've been able to demonstrate the safety, the efficacy, and the long-term data already out to five years.

If you look at the failures in the Nissen fundoplication group, that failure is usually before five years anyway. So looking at a five-year cohort is about all we really need to do to get things rolling.

Nest slide. And we already talked briefly about the eligibility. But, again, this is an area where overall, the aggressive approach to reflux disease is underutilized. A significant number of patients suffer from reflux but not everybody needs surgical intervention. And the gastroenterologist funneled people to the surgeons only after they've passed a certain number of clinical tests to say you're a failure on medical therapy.

The biggest cohort, of course, is the regurgitation patients but not only those patients. Many patients with double dose PPIs that are failing with no particular regurgitative contents still need to be considered for antireflux surgery.

Next slide. We can see that, again, it's showing that there's a very large cohort of patients that don't really get addressed properly, they're offered only medical therapy. But if we have a more suitable surgical option, more people would be able to get relief from their disease.

Next slide. So – next slide. Here, you can see how the device works. Again, it applies minimum pressure of 15 millimeters of mercury around the lower esophageal sphincter which is the physiologic pressure that the rest of us get to enjoy throughout our lives. This device allows the restoration – the exact amount of pressure because it is very carefully measured and implanted. So it's a very reproducible procedure.

The removal is also very easy and it leads you back into the normal anatomy that you had before you went in for the operation. And you can usually – the length of staying is shorter, and the – you resume your activity as much more quickly. So it's something that offers return to work and return to usual activity as much as quicker.

Next slide. We talked quite a bit already about the alternative to the Nissen fundoplication. But I kind of want to go through the things that I think are important for you to consider as you're considering this data.

Next paragraph or next slide. Next slide. So we know that it's at least equal to the Nissen fundoplication in terms of the outcome. So the durability, you can see here, the long-term durability seems to be at least as good as in Nissen fundoplication.

Next slide. It has incredible control over regurgitation. It seems to stay down over the longer period of time.

Next slide. It also helps to keep many patients – most patients off of their PPI therapy. And I would add to that, that patients that go back on any PPI therapy after a Nissen fundoplication generally go back on and never come back off whereas with the LINX system, what I've noticed in my practice and many other people around the country that I worked with in this device, have noticed that it's intermittent dosing, not necessarily going back for forever period of time.

Next slide. The quality of life is considerable. I'd like to share with you a brief story about a husband and wife team. The husband had a Nissen fundoplication 10 years ago. He had urged his wife to come in and have, you know, to have the same thing done alongside of him several years ago, and she refused when she heard about the LINX. She came to see me and I put her LINX in and she had a really good result, which is very common. The husband started having a recurrence, opted to have his Nissen taken down and the LINX put in. It's not uncommon that you see people that

are coming back with recurrences from the Nissen opting to have the LINX put in as opposed to have a redo of their Nissen.

Next slide. Next slide. Next slide. So here are some of the data that you've seen already just to kind of briefly push on the points that I think are really important. A lot of people are worried about not being able to burp or throw up. I mean, I don't personally know why that would be a problem, but a lot of people want to be able to do that. This device allows for physiologic regurgitation, belching, and vomiting.

Next slide. And we already talked about, you know, just in general, how it improves patients' HRQL scores.

Next slide. Similar to the Nissen fundoplication, regurgitation is much better with the LINX. And this is something that stays for the duration.

Next slide. We haven't talked yet about what about the operating time. Well, I can tell you that doing a Nissen fundoplication, if you do it the way that you're trained, it takes a lot longer than with the LINX. It requires mobilization of the anatomy which is often already abnormal. It requires placing the anatomy into an abnormal super physiologic state, something that the body doesn't really want. And it takes quite a bit longer to do even in the hands of people who do it all the time.

The LINX is a very quick, very easy device to insert. And it's very precise in terms of how the measurements are done.

Next slide. The re-operation rates as we have discussed before also very low with the LINX compared to Nissen fundoplication. But the beauty is that if you have to remove a LINX, you remove it in your anatomy is normal. If you have to undo a Nissen fundoplication, you often end up with holes in your esophagus, holes in the stomach, feeding tubes for two months, stents leaks, ICU stays, ventilators, the whole bit. It's a much more difficult secondary – second time through procedure to do if you have a re-operation after a Nissen fundoplication.

Next slide. Significant shorter length of stay. Almost all of my patients will go home on the same day after a LINX. After a Nissen, because it takes a longer time to do it, you're more than likely going to admit people, especially the elderly population, you know, the Medicare population that we're specifically talking about.

Next paragraph. Next slide. It hasn't yet been totally evaluated, but we do expect that the 30-day re-admission rate is going to be very low. I mean I can to speak with many other people that I worked with around the country, very few of us have had any re-admissions from the LINX. Re-admission from a Nissen fundoplication also not very common but not zero.

Next slide. So I would just say in closing that, surgically, this is something that's much easier to provide, to place, and it provides relief. And when patients come in to see you post-operatively, they're much happier with their results. And I think it's really critical that we're able to offer to our Medicare population here the same thing that other Medicare patients around the country are already getting the benefit of. Thank you.

Carolyn Cunningham: Thank you. Questions or comments?

Stephen Boren: Again, Dr. Boren, one question. I did not see a slide which any potential conflict of interest …

(Mary Maish): No, I have …

(Inaudible)

(Mary Maish): No conflicts to disclose.

Stephen Boren: Thank you.

Carolyn Cunningham: Anyone else on the line?

Operator: As a reminder, to ask a question, you will need to press star one on your telephone. To withdraw your question, press the pound key.

Carolyn Cunningham: Dr. Altimari?

Anthony Altimari: Yes. Good morning. My name is Tony Altimari. I'm a general surgeon out in the western suburbs of Chicago land Central DuPage Hospital, which is out in DuPage County.

We've heard a lot of data this morning spoken. I don't feel I'm any need to repeat that. And what I wanted to talk to you this morning is about my clinical experience as

a 35-year experienced of general surgeon who has been doing anti-reflux surgery since early 90s.

The evolution of reflux surgery is fascinating, I think. Dr. Nissen performed the first Nissen fundoplication in 1955. So there's a huge amount of data and understanding of what that procedure is. I didn't – I wasn't alive then, although I feel like I could be. And my experience was back in the 80s. I trained at Loyola. I came out in practice in 1988, to the Central DuPage Hospital in Winfield, Illinois. And in 1992, the first laparoscopic cholecystectomy was performed, and that exploded this area of laparoscopic surgery.

Very quickly then the Nissen fundoplication was adopted as a procedure that could be done laparoscopically. And I want to echo what the previous speaker said, this is not an endoscopic procedure. This is a laparoscopic procedure. And I noticed in the slide, the first slide that was presented on why this was turned down is that it was felt to be an endoscopy procedure. This is not an endoscopy procedure. This is a laparoscopic procedure.

In the early 90s, mid 90s, late 90s, this procedure, the laparoscopic Nissen fundoplication exploded. We were doing anywhere from 100 to 200, sometimes 250 a year, which is four to five a week in my practice. And it became a standard way to treat surgically this difficult to manage medical problem and patients last time to it.

What happened, though, is that as time as this procedure was adopted, there was such a variability in the results. There was such a variability in the success of the operation, such a variability in the number of complications that occurred that slowly, the gastroenterologist and patients decided, I'm not sure this is for me. And all the reasons why it's been described, it's an operation that distorts the anatomy. It's an operation that is not easily duplicated from surgeon to surgeon.

Again, Dr. Nissen, this concept of wrapping the top of the summit around the bottom of the esophagus was brilliant, what a brilliant idea this was. And so he deserves a ton of credit for this. As this has evolved in my practice in the 90s and the early 2000s, I was as a reflux surgeon, doing tons of these, like I said anywhere from 50 to 200 in a year, and then slowly that practice slowed down because of the variability in the results.

About five years ago, the LINX device came along into the community surgeon – again, I'm a community surgeon, not a researcher – as an alternative to the Nissen fundoplication. And the attractiveness there is that it is reproducible and is described it is a relatively simple operation that has done very quickly.

And so what I've experienced in my patient population, I'm back to doing anywhere from 50 to 100 anti-reflux procedures in a year. I've adopted LINX as an adjunct to that. And I find a lot of people request the LINX once a year the data. And the common statement I get made to me from these patients who've had successful anti-reflux procedure, i.e., the LINX device, is thank you for giving me my life back. Because we do not – we cannot underestimate the significant lifestyle changes that occur in someone with chronic reflux disease. And so to offer a cure for this and that's really what this is, this is a cure for reflux disease. All the other approaches are just band aids or masking of the acid. This is a true cure for reflux disease; has been a remarkable addition to my practice.

So we, out in the western suburbs, we do a lot of community outreach. We do a lot of community education. And about once a month for the last several years, I've been doing a community outreach, had dinner with the docs, where we invite community members to come hear about topics and refluxes, one that I present frequently. Now, albeit a lot of people show up and most commonly the Medicare population shows up, and I think it's because we offer a free meal. I think that's the main reason. But I hope that there's other reasons why they do that.

And after our presentation, I have – I get a huge excitement from the Medicare population. And we track these patients and we bring them in and we bring them in for a consultation. And the – it is very disappointing to not be able to offer this to the Medicare population because it can't be paid for. And so that's why I'm here today to reiterate the fact that this is great technology. The data is proven. And, again, I don't feel I had to present any more of the same slides on the good data that's surrounding this. But we need an opportunity to offer this to our patients and the Medicaid – Medicare population that would really benefit from this.

I think that's all I have to say. I would add that I have nothing to disclose. I'm a community surgeon who just works for a living.

Carolyn Cunningham: Questions or comments – thank you. Questions or comments? Any on the phone, (Felicia)?

Operator: As a reminder, to ask a question, you need to press star one on your telephone keypad. That's star one.

Anthony Altimari: Thank you.

Carolyn Cunningham: Thank you. OK, we're going to move to our next topic, which Dr. Boren is also going to present stereotactic radiosurgery and stereotactic body radiation therapy. It's a reconsideration that we need to consider. Steve?

Stephen Boren: Yes. Thank you very much. I hope you can hear me. Yes. We have had a reconsideration for allowing the stereotactic radiosurgery added as an indication, or I should say, choroidal melanoma as an indication for stereotactic radiosurgery. As I mentioned previously because of the new rules about changing or reconsideration of policies, we have to have a formal reconsideration.

And the amount of literature that we received that I could find was not really voluminous. But on the other hand, choroidal melanoma is very common; and to have a very large series of patients wouldn't really be possible. On the positive side, then the papers suggested (different) results on patience after use of stereotactic radiosurgery on choroidal melanoma. So the outcomes were at least as good as all the other methods. Thus, we felt that we should be able to add choroidal melanoma as an indication for stereotactic radiosurgery.

Carolyn Cunningham: Questions or comments for Dr. Boren?

Operator: As a reminder, to ask a question press star then the number one on your telephone keypad. That's star one.

Carolyn Cunningham: Thank you, Steve.

Stephen Boren: OK, thank you.

Carolyn Cunningham: Next we're going to go to hypoglossal nerve stimulation for the treatment of obstructive sleep apnea. And this policy, (Nikita), if we could – here on the slide,

that's good. I listened that we're going to talk about the indications and the limitations and not really the scientific support for it in the interest of time.

The covered indications are that it's considered reasonable when the treatment of moderate to severe obstructive sleep apnea when all following criteria are met. And this is really what the FDA approval was for. So they sure need to be 22 years of age or older, BMI less than 35 kilograms per meter squared, and sleep studies performed within 24 months in the first consultation with implants and beneficiaries, predominantly obstructive events that is less than 25 percent central sleep apnea events.

Next slide. Again, the FDA also made this change that makes the HIV down to 15 and up to 65. And this device is – has been developed for people who cannot tolerate or will not tolerate sleep apnea. Their needs to be absence of the sensory collapse of the soft palate level on a drug-induced sleep endoscopy procedure. And there needs to be no other anatomical findings that would compromise the performance of the device, like (inaudible) and that sort of thing.

Next. The limitations that are considered appropriate are the following – not been studied to use for any other indications. It needs to be FDA approved device. As we said before, the central apnea can't be greater than 25 percent. And the BMI has to be equal to or greater than 35.

I'm not going to read off all of these limitations again. The interesting thing about this device is that, for the most part, the studies that are in the literature has the same criteria of eligibility and the same limitations. And many of them are listed on this slide.

And we can go into another slide, (Nikita). Let's go to the next slide. I mentioned drug-induced sleep endoscopy. This is something that is considered necessary and has been, again, has been used of the studies once the star study developed and in some studies before that. And they basically give people (profit) law and then look to see whether or not the area collapses very (briefly).

Shared decision making is something that we feel is necessary because this is vital. Works for some people, doesn’t work for everyone. And we think patients should know ahead of time what those data show. And also, we've included a requirement

for (inaudible) laryngologist with classroom instruction and cadaver training for an FDA approved technical manufacturer. And the technician needs to be trained on the titration device. And we also have certain restrictions on the sleep studies that are in an article that's listed there.

Questions or comments?

OK, we're going to go to the first presenter, which is (Kathy Sherwood).

(Kathy Sherwood): Good afternoon. I'm (Kathy Sherwood). And if you move on to the next slide, I do have a disclosure, I work for the company. So I lead the market access and reimbursement team. And I'll just begin by saying, we are really pleased with this LCD. We are pleased with the new process at Medicare, and the fact that we have collaborated to present the evidence. And we feel that this has been a really excellent collaboration between all of the Medicare MACs and industry. So thank you very much for that.

Next slide. We have just a couple of comments, and I hate to call these housekeeping but almost at that level. We're very comfortable with the coverage criteria because as Dr. Cunningham said, it matches the FDA approval language and that's exactly as it should be.

There's a few things that as industry we would like to touch on. And the first is the drug-induced sleep endoscopy training. As we mentioned, industry is going to actually – we do perform both implant training as well as (DICE) training for any physician who get certified by the company. And this actually goes into our quality system, which the FDA monitors annually. But we perform that training in certified physicians. So we have a proposal for how to do the drug-induced sleep endoscopy training that we think logistically will be tighter and basically more easy to manage.

And then we just have one comment about the price interaction statement because it actually has been tested and approved by the FDA. This device can be implanted with defibrillators, pacemakers, and everything else that, that testing has been performed. So we suggest that maybe that's not an appropriate limitation.

OK. So, next slide. So I mentioned the overview of our physician (DICE) and implant training and certification program. (DICE) is a subjective test. But it's the best way to

tell which patient is really going to be most appropriate for this therapy because it's taking a deep look at the upper airway anatomy and looking for basically absence of full concentric collapse in that upper airway.

And so we think it's extremely important that physicians are properly trained to do this. And given that it's subjective, we in fact have a module of training that they take along with cadaver training, where the physician will actually perform some dice, send it up to industry, and then we have a team of physicians that help us review these dice and basically say, yes, you got it right or, no, you didn't. So that's that second level service.

We go to the next slide. OK, so the current (DICE) recommendation or the draft policy basically says that industry – that the physician, who would like to become an implanter sends 15 dice up with the video clip, and we would do a review of that. And they would need to get 80 percent of them to match what these experts say. And then that would be documented.

And we actually agree with the intent of this. We're good with that. But what we are proposing is that our current training program is to basically do five of these. So we're OK with adding an additional 10. But we're proposing that we do that by basically having a prerecorded group of complex dice that would be performed or basically given to the physician as like a computer-based test, as they're doing their cadaver training. So they could do 10 of them where we know what the right answer is, but they're still essentially reviewing that video clip and getting the answer right; if not, then they go back to the drawing board and retrain.

And then the last five would be consistent with our current training program, where they send those in before we give certification. And it is important to note, we will not distribute product. We're the only FDA approved manufacturer at this point. We will not distribute product to a physician that does not have the certification because if we get bad outcomes, our company goes out of business. That's the way we look at it. This is critically important that this therapy works and we get the right patients.

So, OK, and next slide. And the only other comment that we have here is that there is a statement that says that these implantable devices could experience on intended

interaction. And each of the Max who have posted a positive draft coverage policy has the statement. But in fact, extensive testing was performed.

We were actually – our company spun out of Medtronic. And so we had extensive testing performed to validate that in fact, we do not interfere with other neural stimulators, with defibrillators, pacemakers, and other infusion pumps and that type of thing which was all submitted to FDA when we got our was our original lab, PMA approval. So, we suggest that maybe that limitation be reconsidered. OK.

Next slide.

Carolyn Cunningham: That's it.

(Kathy Sherwood): OK.

Carolyn Cunningham: Questions or comments in the room, on the phone?

Operator: As a reminder, to ask a question, you would need to press star one on your telephone keypad. That's star one.

Carolyn Cunningham: Thank you.

(Kathy Sherwood): Thank you.

Carolyn Cunningham: OK, next we have a couple of presentations by phone. And the first is Dr. Suurna. I'm sorry if I mispronounced your name. Are you there? Dr. (August Smith) are you there?

Female: Operator – yeah.

(August Smith): I'm here.

Female: OK. All right. Is that Dr. (Douglas Stina)?

Carolyn Cunningham: Operator, can you just check to see if they are on the line, please?

Operator: I don't see that line. What was the first name?

Carolyn Cunningham: (Su).

Female: Maria.

Carolyn Cunningham: Maria Suurna, S-U-U-R-N-A.

Operator: One moment. Maria Suurna, you may go ahead.

Maria Suurna: Can you hear me now? Is that …

Carolyn Cunningham: Yes.

Maria Suurna: OK. So thank you for the opportunity to discuss this LCD and decision. And Dr. (Augustine) and myself will – we have the combined slides. We'll address the points together if that's OK. And I'm with Weill Cornell Medicine, my EMC surgeon who is board certified in otolaryngology and sleep medicine. And Dr. (Augustine) is with the Middlesex Hospital and he's also board certified in otolaryngology and sleep medicine.

Next slide.

We do – we are enrolled in a post approval clinical trial with Inspire and have received honoraria from Inspire Medical, mostly for speaking engagements.

Next slide please.

So there's a couple of aspects that we would like to discuss. One of them actually pertaining to share decision making. There is several instances where there is referrals to shared decision making, by referring providers to sleep medicine providers, and otolaryngologist or implanters.

So that has to be a little bit more qualified in terms of what's your decision making constitute because as otolaryngologist, especially if you're board certified in sleep medicine, we manage patients from the very beginning like starting with diagnosis, sleep apnea, providing feedback management, oral appliances, and we manage their CPAP failures. And then in some cases where non-surgical treatments fail, we offer surgical procedures and the evaluation for surgery.

A lot of times patients actually come to us after struggling with CPAP for years or have not used a CPAP. And a lot of times their sleep medical physicians we're not like a no longer in the picture, a lot of patients are referred to – self referred to us.

And so as otolaryngologist, actually, well versed in sleep apnea and management and such. So in terms of getting like, you know, supported documentation for a sleep physicians or referred providers that might not even be available in scheduling the consultation with three physician who is not otolaryngology might be more like to take out more time and actually might not be efficient.

And it's also cost beneficient and also in terms of patient care, it's just – again, provide various for patient management, treatment of certain sleep apnea. So if there's a documentation from primary care physician or referred providers that's available, that's great for medical history, completeness.

But it's all of that can be found from otolaryngology notes. And there's actually there's a good documentation on feedback compliance and feedback trials and failure and discussion of alternative, then I don't know, I don't see how shared decision should be required. So we would like to consider either removing it or adjusting it. So that actually clarifies and doesn't limit patient access to the therapy and treatment.

Next slide, please.

So on drug-induced sleep endoscopy, so I know. (Kathy Sherwood) has addressed the details of drug-induced sleep endoscopy. So it's a flexible endoscopy while patient is sleeping. So patient is done under sedation as a quick procedure. It doesn't really differ much from a technical standpoint, as other nasal endoscopy, so laryngoscopies, or esophagoscopies that we'll perform. And all of these, like all these endoscopic procedures are basically part of standard otolaryngologist practice.

And I don't see how drug-induced sleep endoscopy actually is that much different in terms of like no evaluation like what we're looking for? Yes, there could be like a video training videos and could be like a brief instructional sort, of course online or provided to us. But I don't see why this procedure has to be very different from other endoscopic procedures that we already perform and requires some extra certification and especially most of us get exposed to it now in residency, since it has become pretty widely available procedure.

And I don't think that special certification should be required, especially by the manufacturer because again, people from a manufacturing standpoint they are not

physicians. And so in some of the procedures like endoscopic procedures and then also in terms of training, I think, like you get trained and residency and, again, I don't see that excessive certification should be indicated because again, that drug-induced sleep endoscopy, it is not from technical standpoint much different from what we already do.

Next slide, please.

I can you also can also request, Dr. (Augustine), is actually – also Nicole and I don't think his line is open. Is it possible to open his line as well? And his number is 860-2807-235. Is that something that's doable?

Carolyn Cunningham: Operator, can you assist with that please?

Operator: Yes, ma'am, one moment.

Maria Suurna: So he can also participate in this call.

So, while Dr. (Augustine) is joining, I'll proceed to the next slide then if that's OK.

So the other proposed indication is that under covering medications is that the anatomic findings, specifically focusing on tonsils the size three and four based from tonsil (inaudible) grading. Well, that should not be contraindications because of some of that could be subjective. And again, there's no evidence that tonsillar hypertrophy is contraindicated for the loss of our simulation and it actually can significantly alter the outcome.

For example, some people actually can have tonsillar hypertrophy that’s transient due to inflammatory process or respiratory infection. So, I would suggest that we leave that up to the implanters. And again, please do evaluate anatomy on the routine basis. And I don't think that this type of an atomic consideration should be considered as a contraindication to the device or to be implanted to the therapy so we suggested consider removing it.

Next slide.

So the other – after that being discussed are limitations. And there are several limitations that were listed but specifically the ones that we wanted to make sure that

they're clearly addressed or modified is like for example, active (psychiatric) disease, which again, what is it defined active psychiatric disease is that depression, anxiety, which often are exacerbated by sleep deprivation and sleep apnea.

And that should be like no patients are well managed and properly treated with like anti-anxiety or antidepressive medications they should be a candidate for this therapy as well as their association with untreated sleep apnea and development of anxiety and depression for example. So again, that should be clarified.

And neuromuscular disease, again, that should be more specified a little bit more even more detailed what's considered neuromuscular disease. For example, like in the peripheral neuropathy, sciatica, like sweat drop, some of them neuromuscular disorders that contributes to the neuromuscular tone issue, like for example, in Down syndrome patients, I mean all of those things can be great candidates for patients to still continue with therapy. So that needs to be addressed and adjusted to reflect what type of specific neuromuscular disorders we are discussing.

Also uncontrolled hypertension, again, that needs to quantified what is considered uncontrolled hypertension because again, a lot of patients have poorly controlled hypertension due to untreated sleep apnea. And then that should not be in a limitation for implantation.

There's also another subject that's not on the list when it comes to pregnancies, this device is not unsafe in pregnancy. So I think it's a surgical procedure that patients who are pregnant or (inaudible) to become pregnant within like, you know, like next few months or so that's sort of like no should not be getting surgery during that time. That should be considered but, again, in terms of the devices being unsafe in pregnancy that should not be saying as such.

So the next – (Mark), are you there?

(Mark Augustine): Maria, we've been trying to get on the whole conversation. Can you hear me?

Maria Suurna: OK, so (Mark), do you have any comments on that you think that I've gone through so like before we proceed to the next one.

(Mark Augustine): No, I just wanted, I just wanted to reiterate what you said about the shared decision making, I think that should be made between the physician and the patient, as

opposed to a referring provider. As you mentioned, Dr. Suurna, mostly referring providers are not as familiar with this procedure or the indications or qualifications for it as we are.

And a lot of these patients come to us as the primary modality of treatment. And as we are doing CPAP ourselves and trying to get some patients to use CPAP, if there are failures, we're trying to offer them another service and to try to get approval from a referred physician who may be totally unfamiliar with the patient or their situation or the actual procedure itself, I think is uncalled for.

And then the second indication I want to make or comment was about the drug-induced sleep endoscopy as Dr. Suurna had said, I mean, we were doing drug-induced sleep endoscopy with long before Inspire came along. This is what much as we do nasal endoscopy and other procedures in our field. So I mean, it seemed a little redundant or strains to have industry certify us on a diagnostic procedure that we're already doing.

And I agree what you said as far as the anatomical requirements and where you are in this current slide Dr. Suurna, if you want to continue, sorry to interrupt you.

Maria Suurna: OK, so the next (service innovation) is it's about the device model (3024) that's just basically irrelevant because I don't think this model is longer available. It's no longer on the market. We're no longer implanting this model, so that should be removed.

Next slide.

So, next one is talking about qualified physician who is board certified otolaryngologist, complete the appropriate AMA or AOA certified residency and fellowship program and maintain ongoing certification otolaryngologist. So this needs to be modified.

It should be board certified award eligible otolaryngologist, because it has – it's division has to be at least for a year in practice before they take their boards, so young physicians should be able to have the opportunity to offer this therapy even within their first year of after training.

And then the other thing is that we don't usually – there's no fellowship training for this. So residency in otolaryngologist – completion of residency should be sufficient to qualify for this type of procedure.

Next slide.

So the (inaudible) receive classroom instructions by the approved device manufacturer or equivalent on device implant techniques as well as cadaver training. So initially, yes, the cadaver training was essential, what the procedure was first developed. But now since we're doing it more and more and a lot more residents are getting exposed to this in their residency training, if there is a significant training in their residency, I'm not sure if cadaver training should be mandatory for all of the physicians especially when they actually had like most already done or observed or participated in like techniques like, you know, about 5 to 10 implant.

So should some modification need for (inaudible) implant, if they were available in residency or fellowship.

(Mark Augustine): I agree if I may join in there, Dr. Suurna. I think that, you know, this is a procedure that involves a part of the anatomy or part of the neck that we are in all the time for head and neck cancers and removing salivary glands and whatnot. And so, most – anybody board certified in otolaryngology should be very well familiar with this anatomy, in this area, the nerve itself and other than the industry training on the actual device and how to put the cup around the nerve. I'm not so sure that cadaver training would be necessary for something that's already well versed in this anatomy.

Maria Suurna: OK. Next slide. So the next one is the (inaudible) referral on post-implant evaluation that happens lots of (nursing leader) but not excluding (inaudible) certain physician should be performed by board eligible or board certified sleep physicians with qualifications as outlined, typically so that's (sleep) technicians. And then so sleep study should be performed in accredited sleep facility as stated in the article.

So, we basically suggest that should be performed by a physician qualified to teach patients with a sleep disorder not necessarily stating likeness certified sleep (physician). Because again, as an otolaryngologist especially as implanters, we do manage patients and we do prescribe – set him up with the sleep studies and we do activate the device, we do adjust the device.

So a lot of times if otolaryngologist are comfortable and available and again should be the primary of – should be – I guess not necessarily primary but should be available and to provide the sense of care, and a lot of times, we are the first ones to actually initiate and deal with this therapy.

And the same – and the same way when we talked about, you know, sleep setting, the facility, yes, in certain situations in the lab, case studies should be done for patients to evaluate the other therapy effectiveness. But in a lot of situations we can actually evaluate patients with a home testing especially when it's in terms of like, you know, following up like a long term follow up and after the settings adjustments and just looking at the effectiveness of therapy. In many circumstances, we don't need to have like mandate to have a sleep study performance in a sleep facility.

(Mark), Dr. (Augustine), do you have any comments?

(Mark Augustine): Yes, no, I agree. I mean that the titration study needs to be done in the lab, but following these patients with a home study is very appropriate. And in addition here I think that – I think there's two models that we see with the Inspire therapy. I think there's the model where the otolaryngologist or the sleep certified otolaryngology is very comfortable with this and handling the patient and managing them and controlling it. And I think there's a model in some centers where this – the internal medicine, sleep physicians are, you know, are very involved and they will refer the patient for implantation and then they'll see the patient back to manage them or to titrate them.

So I think to be very – to be restrictive in the wording as to who's going to follow-up and take care of the patients is not appropriate. I think that it should lead, you know, by a qualified physician in handling measly patient whether that is a board certified sleep physician, or a board certified sleep otolaryngology physician.

Maria Suurna: I think that's our last slide.

Carolyn Cunningham: Is there other questions or comments? On the phone.

Operator: As a reminder to ask a question, you will need to press star one on your telephone keypad. That's star and the number one.

Carolyn Cunningham: Thank you very much. We are now going to move to our next policy which is Salvage High-Intensity Focused Ultrasound treatment in prostate cancer. Dr. Howard is going to present.

Craig Haug: Yes, good afternoon. Can you hear me OK?

Carolyn Cunningham: We can, Craig.

Craig Haug: OK. So this is a new policy with title Salvage High-Intensity Focused Ultrasound, HIFU for short, treatment in prostate cancer. The salvage denotes we're talking about treatment after recurrence after primary therapy. And so the reason for this procedure is that a certain amount of patients who – whose primary treatment is radiotherapy relapse. And it's about half of those patients and about a quarter of relapse in a localized fashion and this relapse can impact mortality.

There's no standard of care for such patients currently although radical prostatectomy is probably the most accepted. There's interest in potentially less invasive alternatives such as like the (therapy), cryoablation and HIFU which is again the subject of this policy.

Next slide

HIFU is a energy based minimally invasive ablative treatment. A transrectal ultrasound probe is place with which both images the prostate and delivers the burst of heat to create coagulation, the closest in that targeted area verified by the ultrasound that is surrounding cooling balloon that protects the rectal mucosa from the high temperature. It's done as an outpatient and a spinal or general anesthesia.

And next slide.

Results are generally similar between HIFU and radical prostatectomy with perhaps the data we have showing. And so far showing perhaps more urinary incontinence and erectile dysfunction after radical prostatectomy.

Next slide.

So in summary, there's no level one data. All the data is there are several observational study, some are prospective, some of are retrospective almost all are

non-comparative and relatively small with short follow-up and non-standardized outcome measures.

On the other hand, while the quality, the data is cumulatively moderate in size and generally consistently positive. If you look at the various guidelines nationally and internationally, the recommendations span the continuum from saying there's equal results with radical prostatectomy so parity to relegation to experimental status. Basically all the guidelines do recommend or endorse radical prostatectomy.

So we took the compromised position of limiting salvage HIFU to high comorbidity patients that would otherwise be eligible for radical prostatectomy.

Next slide.

I'm not going to go over these, but suffice it to say that the generally outline the criteria to be a candidate for salvage radical prostatectomy except for number five that high comorbidity i.e. not a candidate for radical prostatectomy that I just outlined. So as I said who otherwise would be a candidate except for that. And these are generally accepted criteria for salvage radical prostatectomy.

I think that's it. Any questions?

Carolyn Cunningham: I know there's any in the room. Are there any on the phone operator?

Operator: Again, in order to ask a question, press star one on your telephone keypad. That's star and the number one.

Carolyn Cunningham: OK, thank you. Next we have (Mr. Embert) – (Dr. Embert).

(Mr. Embert): No, Mr. Thank you. Thank you very much for giving me the opportunity to discuss with you Savage HIFU for the treatment of prostate cancer. Hope everyone hears me well on the phone.

Carolyn Cunningham: Can you hear in the back?

(Mr. Embert): Despite the accent, sorry. So I'm an employee of one of the manufacturers of HIFU devices, so that's my conflict of interest, obviously. What I would like to do is, is present quickly the HIFU technology and (deterring) clinical evidence in the treatment of prostate cancer that led to this LCD. But also I want to discuss the

stress article for HIFU, the salvage therapy and potential negative impact that could have on the coverage of HIFU for other indications in particular primary prostate cancer.

Next slide.

So the principle of HIFU has been explained. It works a bit like the magnifying glass with the rays of the sun that focuses the rays of the sun to burn the leaf. We do exactly the same. We regenerate ultrasound, but we focus and then point to elevate the temperature and create a calculation it closes so it burn, basically, remotely tissue.

So we do this through the rectal wall, so it's a completely non-invasive procedures instead of opening to take the prostate out, we can focus the ray of the sun to destroy part of the prostate where the tumor is located.

Next slide.

In terms of regulatory status, this – the principle of HIFU has been studies for more than 50 years actually. But as far as prostate cancer is concerned, it's been approved in Europe for about 20 years now along with other countries around the world. But it's been only recently approved by the FDA. So, a few devices have been cleared initially towards the end of 2015. And more recently, the latest addition to that group of devices clear here in the U.S. is the focal one.

Next.

HIFU adoption around the world. So there's been more than 70,000 treatments of prostate cancer with HIFU. The majority – the vast majority of those are primary prostate cancer patients that between with HIFU focused ultrasound here in the U.S. because of this late clearance we estimate about 3,000 patients treated so far in the past couple of years.

And once again about 95 percent of patients were treated for primary prostate cancer treatments at large academic institutions that acquired the devices, but also some ambulatory surgery center. It's an outpatient procedure. And as I said, the majority's first line, a little bit of salvage and whole-gland and partial gland more and more partial gland ablation one of the pluses of this technology, this ablative

technologies to be able to destroy part of the prostate where surgery cannot do, because surgery can only take the whole prostate out or gland.

Next slide.

In terms of reimbursement, so CMS has created a HCPCS code towards the middle of 2017. That was initially URGBC level six been determined shortly after as a device intensive procedure, around the same time, NCCN guidelines have included HIFU as a recommended therapy for radio recurrent prostate cancer. So at the same level as a surgery and cryotherapy for those patients which lets them probably three years to start covering for HIFU in this specific (salvage) setting.

And first Medicare administrative contractor issued positive LCD across an article actually for HIFU in the same (salvage) setting last year. And they are actually retiring it as we speak because of the unintended side effects that we'll discuss towards the end. It's covering only salvage.

And last but not least, recently the EMA because of the wide body of evidence awarded HIFU with a CPT Category 1 code which will become effective January 1st, 2021. So, HIFU even if it's pretty new therapy in the U.S., it's been out there for a long time outside of the United States. And there are more than hundred peer reviewed publications covering different utilization of HIFU prostate cancer, long term large cohort, multicentric, some looking at primary prostate cancers and looking at salvage whole-gland, hemiablation focal therapy.

I'm not going to go through whole 100 patients or more. Just look at a couple of salvage publication. The first one which I think which is one of the largest one in the salvage setting, 418 patients that all had a primary radiation therapy that failed and were treated by HIFU. And about 81 percent of those people were free of metastasis seven years after the HIFU treatment which is remarkable for the setting of patients that have the regressive disease that already failed the first line of treatment.

Next slide.

The combination of this last cohort European series of 400 patients and this paper and hundred patients treated this year in the U.S. and in Canada as part of an FDA trial which is shorter term, but the combination of the two article led the NCCN to

include this indications as a standard of care for salvage patients. As well as I think lead to this article in LCD that we're talking about today.

Next.

So HIFU as I said that is not limited to salvage and actually the vast majority of the literature is for primary patient first for whole-gland therapy. There's a number of large cohort of patients that have been – six consecutive patients that have been studied. And you can see throughout articles from different countries and different groups totaling up to 17 years of follow up to some of them that the 10 year cancer specific and the metastasis free survival is extremely high even for intimidated high risk patients that have very aggressive disease.

And click please, can you click on this? Yes, so next to that you have the similar numbers for the prostatectomy for the series that were published by the Mayo Clinic and the Memorial which are state of the art prostatectomy centers here in the U.S. So you see that the long term efficacy of HIFU is on par with the radical prostatectomy which led to the wider acceptance of HIFU at least in Europe and today here in the U.S. calling (Excite).

Beside these whole-gland treatments, so the past 10 years because of the improvements and the ability to detect with MRI, to detect where the cancer is located inside the prostate, phototherapy is – has been growing and growing. One of the publication which is one of the publication that led the EMA to award this CPT category one code is a meta-analysis following the PRISMA methodology which has a level 2a evidence that filter down seven cohort study with up to 366 prostate cancer patients that all had a part of their gland treated with HIFU.

And very – all the studies are very consistent in terms of numbers, in terms of results. And what is very remarkable is the side effect profile of the therapy about 96 percent – ranges from 91 to 100 percent of the patients are completely (common), (CAT) free for the record with prostatectomy in the first few months about 70 to 80 patients have to wear pads. It improves a long time, but even one or two years after, you still have a good 20, 30 percent of the patients that still have to wear pads after a radical prostatectomy.

And same thing of the potency, there is a potency preservation of the patients with this focal HIFU of around 80 percent of the patient throughout the whole literature, which is once again remarkable compared to what is achieved by with radical prostatectomy with barely 20 percent of the patients are able to have erections without any help from Viagra or other medications of that type.

Next slide.

So this is another, another publication that have very similar that echoes really this kind of – this kind of results and show the stability of the results for focal – for focal therapy. I'm not going to go into details but I have two other publications that I really wanted to highlight. The next one is very recently.

Next slide please.

Is a – is a multicentric – it just came out last year, so was not included in all these reviews, multicentric focal HIFU with 625 patients. Once again the (CAT) free continence and the potency preservation is remarkable. It was expected, but it's consistent from one group to another and it gets with larger – larger populations. And the stability of – we start to have metastasis pre-survival, cancer specific survival at five years for patients that have for the majority of them an intermediate or high risk disease.

So we're not talking about low risk patients, so with cancer patients here talking about 84 percent of them as intermediate or high risk patients. And recently if you go to the next slide, hot off the press, another group in Europe has come out with his own series of more than 1,000 patients. And you can see that even at eight years of follow-up 97 percent of the patients are – the overall survival was 97 percent.

And was pretty remarkable at 81 percent radical treatment free survival, so they didn't need any other treatment. They still oncologically completely perfect and they have very similar side effect profile. And they even show an improvement along the time when the improvement of MRI and imaging that helps target even better the cancer inside of the – inside of the prostate.

Next slide.

Just to go back to the comparison with the standard of care which are radical prostatectomy and radiotherapy is to compare one of those latest papers with HIFU in the top column – on the left column with the latest – the latest results that came up in the New England Journal of Medicine from a randomized clinical trial between radical prostatectomy and radiotherapy in the UK. We can see the disease control of five years are extremely on par – are on par with HIFU with the radiotherapy and radical prostatectomy with a far better side effect profile.

And you can see and of note if you look at the top rows, you can see the HIFU patients had a far more aggressive disease, 72 percent had a grade in seven and higher. Prepared to do radical prostatectomy and radiotherapy where the majority of them are very low risk patients.

Next slide.

So as a conclusion, what I want – the message I wanted to convey is that HIFU presents a wide body of evidence, thousands and thousands of patients, hundreds of publications through publications that clearly support the safety and the durable effectiveness of this therapy, not only as a salvage, but also for first line patients in both whole-gland treatment strategy or a focal strategy.

Back to the reason we hear NGS proposed a LC, an article for salvage, we – we all believe that's a step in a positive directions, policy direction. But we want to make sure – we want to make sure and we're pretty concerned because of the WPS experience, that this will not preclude a case by case processing at least for the claims of HIFU for initial treatment of prostate cancer, which is the case today.

And last but not least, we would request of course, that all that new evidence on primary prostate cancer would be considered and looked at by NGS for an extension of this LCD or a new article.

Carolyn Cunningham: Thank you.

(Mr. Embert): Thank you very much. If you have any questions, questions.

Carolyn Cunningham: Questions, comments?

Craig Haug: Carolyn, I have a couple questions …

Carolyn Cunningham: OK.

Craig Haug: … for Mr. (Embert). Mr. (Embert), you presented a lot of information there. You alluded to some new studies, I mentioned that there was no level one data, none of those recent ones are level one neither are they?

(Mr. Embert): No, no as – as it was pointed out for one of the other topics earlier today. It is extremely difficult or quasi impossible to randomize a non basic therapy such as HIFU with a radical prostatectomy, but the choice of the patient – some groups are trying and have tried and most of the patients drop out of the – drop out of the study as soon as they're drawn into the prostatectomy arm.

So it's, it's extremely difficult so the best we can do is either propensity score matching or meta-analysis like we have so we're – I think with those 2a level of evidence that's where – that's where we stand as we speak

Craig Haug: And one of your earlier slides mentioned, alluded to NCCN endorsing HIFU for radio-recurrent cancer, I didn't see any other anything else. And NCCN does not currently endorse HIFU for primary therapy, correct?

(Mr. Embert): Correct. NCCN has not – has not updated their guidelines recently on the prostate cancer side. So, so there – they haven't mentioned the primary yet.

Craig Haug: Well they update them every few months. If they pull out, I'd have to look with the last one within the last few months. It was version four, three or four 2019.

(Mr. Embert): To my recollection it was early 2018. You could be right and I'll have a look on my side.

Craig Haug: Yes, I think there's version three or four in 2019. That's all I had, Carolyn.

Carolyn Cunningham: OK, anybody on the – on the line, anybody else on the line that has a question or comment?

Operator: As a reminder to ask a question, you will need to press star one on your telephone keypad. Again that's star one.

Carolyn Cunningham: Operator, could you please include or comments when you are asking people to press star one? So question or comments.

Operator: Yes, ma'am.

Carolyn Cunningham: Thank you. OK, we have two more to go.

The next one is Fluid Jet Systems the Treatment of BPH, OK.

Male: We're supposed to have one more …

Carolyn Cunningham: I'm sorry. My apologies, Dr. Shalhav. Operator, do we have him connected?

Operator: What was the name?

Carolyn Cunningham: Shalhav.

Operator: OK, your line is open.

Arieh Shalhav: Well, hi. So I was listening, just as the introduction. I'm a urologist. I'm the Chief of Urology at the University of Chicago. And I've been a urologist since 1996. And two disclaimers. Number one, I have no financial relations whatsoever with (Focal One machine). So this is one. The second one, kind of to add hopefully some credibility to what I'm going to say is that when I finished my fellowship, I joined Indiana University in Indianapolis, when they were working on their BPH indication for HIFU with focal surgery, what is now Sonablate.

And I as my research during that time, I was interested in kidney and I said, OK, can we work with this role for kidney and see if it works on kidney? So I had a very, very productive, you know, scientific research related to HIFU and my knowledge and understanding on HIFU. And actually the first human trials with the kidney were done in Vienna where I got the code with the company and sat down with (Mar Gerber) who was the head of urology there. And we did a few patients where he was using – we were using the HIFU probe laparoscopically and then he would do a nephrectomy and we would look at the effects on the tissue.

Bottom line it didn't work because I think the kidneys are very difficult site to do it because of the angles, laparoscopically you can't cover the entire tumor. But that's my background with my experience with HIFU that started a very, very long time ago.

So now to my experience with HIFU, I would add that since then, when I moved to the University of Chicago in 2001, I've been watching the HIFU technology and kind

of waiting for it to become good enough to be used where I, you know, I like to sleep well at night and I don't like to have any questions to myself did I do the right thing. So – and I didn't feel that it's ready in the early 2000s to do HIFU on patients.

Obviously not for kidney, but not for prostate cancer. And I was watching it, you know, reading all the science around it and the publications, looking for level – high level evidence and so forth, not happening. And as you know, in many things in medicine, you know, robotic surgery start with zero, zero level one evidence and eventually, you know, became approved and established way before we had them. Now we have level one evidence and obviously, it was true.

But going back to the HIFU, I was watching it and waiting and nothing, you know, was convincing enough that I would say OK, this is something I do want to try for my patients. The last iteration before the Focal One machine, started catching my attention and I started watching people performing it.

Going around, I was in Canada, I was in New York. I was in Germany, and watched people use different machines and different companies to do it. And the final kind of decision for me was once Focal One was ready, and I saw it in action. I was happy to say to myself, OK, now we have what we need to do a good job. And what I think now about the Focal One, that this is a system that delivers very precise energy to exactly where you want it with real time imaging, you can or you can decide to couple it to the MRI or not. But I in a very consistent way, still that we're getting the tissue that we want to ablate destroyed very, very well.

And the studies that you have out there from Europe are mostly done on patients where they did – the whole-gland with the previous iterations of HIFU machines and the outcomes were not great, they were OK. The procedure took a very, very long time. The surgeon should not – the operator should not take his eyes off the machine and it was four hours that they needed to be looking at the machine without any interruptions, no e-mails at the same time or texting. And it wasn't done this way. And they were, I think many handicaps to the system compared to what it is right now.

And that's why the initial results are not as good as you know, I wanted it to be before I offered to somebody. So that's one thing that the evolution of the technology

in the last five years was such that I'm feeling very comfortable now with this technology.

The other concept that changed is the focal or hemiablation versus whole-gland ablation. I don't think the machine is ready to do a full gland ablation yet. I think it's a perfect machine for what we call hemiablation where you take half of the prostate, and keep half of the prostate.

The whole idea of doing focal therapy where you take, you know, a pea sized tumor in the prostate that only treat that and leave the rest of the prostate being, I think is a mistake. You need a margin of about 10 millimeters around that lesion to make sure that it's completely destroyed. And that means that basically if you need 10 millimeters on each side, you are going to do a hemiablation as a minimum.

So people started doing it and there's more and more data accumulating today on hemiablation, where you successfully destroyed one half of the prostate. In my clinic, about 25 percent only of the patients are eligible for hemiablation because their disease is unilateral. Significant disease is unilateral. But for that patient population, I think this now has become a very, very minimally morbid procedure to take care of the tumor without damaging their continence and without damaging their sphincter muscle and the nerve if you want to.

And I actually I'm not shy to say if there's only MRI, extraprostatic extension right by the nerve, I tell the patient, I'm going to cook that nerve together. And with the machine as it is today, I can very, very securely include, you know a centimeter of tissue right on the nerve and together with the prostate, take the nerve, or in cases when the nerve is not involved and the tumor is a little away from the nerve, say, I'm not going to include the nerve and save the nerve.

So I think that the morbidity well, that's what I see, I've done 16 patients full disclosure starting in May 18 of this year. The problem is that, you know, they need to pay out of pocket most of them and it's not easy to get patients to do it. And hence, you know, the effort today to get it to more people, I strongly believe that we can deliver very good care without disrupting the lives of the patients the way we do with both radical prostatectomy or radiation.

And HIFU will find its place. It's only a matter of time, we may not do well this year, with regards to the approvals and so forth. It's only a matter of time where HIFU will find its way, its domain between active surveillance and the very aggressive options that we have which are radical prostatectomy, or radiation, which we should save for people with bilateral you know, high grade disease.

And one last thing I want to say I know I'm talking a lot, I would say that if cryotherapy is an approved procedure for prostate cancer today, there's absolutely no reason that HIFU, the level of delivery that we have today with a Focal One would not be. I pause here, because I'm sure that you guys want to ask me some questions.

Carolyn Cunningham: Yes, that's clearly …

Craig Haug: Carolyn, I just wanted to ask Dr. Shalhav he mentioned his historical connection to this technology, but did you have any current or recent conflict of interest?

Arieh Shalhav: That was the – my initial disclaimer, I never ever had in all my career, I have never (married) industry to – and I do a lot of robotic surgery, so intuitive using the picture and other things, never had any conflict of interest.

Craig Haug: OK. Thank you.

Carolyn Cunningham: Other questions?

Operator: As a reminder, to ask a question or make a comment, you will need to press star one on your telephone keypad. That's star one.

Carolyn Cunningham: Thank you, Dr. Shalhav. OK, next we'll go to the – to the LCD that I mentioned earlier, the Fluid Jet Systems in the Treatment of BPH, OK.

Craig Haug: Yes, this is another new policy. The rationale for this policy is to have a TURP alternative, I don't know if other people could hear that sound but probably nothing we can do about it. TURP alternative with a more favorable safety especially sexual function profile, and convenience as well, more convenience compared to TURP.

So this is a receptive procedure, not an ablative procedure like TURP is. The only FDA cleared fluid Jet System is the AQUABEAM system right now. It is a

transurethral approach using high velocity saline jet and a real time ultrasound, TRUS ultrasound to basically map out the specific region to be targeted by the high velocity saline jet.

So – and a lot of this is done – by computer the resection limits or computer generated, but the surgeon is ultimately responsible for accepting those or not accepting those and then the resection is then executed automatically via robotic arm. The hemostasis is via electrocautery or traction. I think the early reports use more electrocautery and physically then they try to (adhere that and adjust it) to the three-way catheter. The idea is that minimizing heat damage to the erectile tissues, erectile nerves theoretically is advantageous in preserving, you know, sexual function.

One of the notable things that make this stand out is that there's a very short operative time, a mean of 33 minutes. And actually the resection time is even significantly shorter that, meaning, does not seem to be – seems to be almost size independent. So once this thing is locked in, in terms of a mapping, the machine pretty much, the robotic machine pretty much doesn't stay in quickly regardless of the size.

Next slide.

OK. So the evidence here, there is level one data. The main data is a single level one study that is now out to two years. It shows not inferiority to TURP. In functional indices, IPSS, Qmax, quality of life, post-void residual and so with outcomes bleeding (inaudible) urinary retention, UTI, et cetera, and reduce sexual dysfunction.

Next slide.

In summary, there's promising short-term single study results that have resulted in (SS) conditional recommendations and some guidelines and they're listed there. A conditional recommendation Grade C, by the way translates to an unclear balance between benefits and risks. There's a Cochrane Review which says any recommendation for against Aquablation will be based on only very low certainly evidence. And this is basically down rating of the existing evidence that I just referred to for various forms of potential bias. Despite it being a level one study and also some imprecision in terms of the wide confidence intervals.

EAU Guidelines stopped short of even a conditional recommendation. There is no current commercial or Medicare insurance coverage that – which I'm aware. And so, for now, we're considering this still investigational pending publication of what we generally considered to be legitimate midterm, which is defined as three-year result.

I think that's it.

Carolyn Cunningham: Thank you, Craig. OK, we have two presenters in person and one on the phone. Are you Dr. Helfand?

Matt Salkeld: No. Dr. Helfand is next? Is it possible for the next from – for my presentation to go next first? I'm Matt Salkeld.

Carolyn Cunningham: I think she can do that later on the hour.

Matt Salkeld: Thank you very much. Thank you. My name is Matt Salkeld. I want to thank the NGS for reviewing the clinical literature and the guidelines as well. And I appreciate the opportunity to comment.

Next slide.

I am an employee of the company. And during the next 10 minutes, I really want to focus on three things. One is talking about the fact that this – Dr. (Hogg) mentioned the two-year clinical data was published. It's a randomized clinical trial against TURP, which is the gold standard in BPH. That was published subsequent to many of those guidelines being established and are not reflected in those guidelines.

The second thing is answer some questions on some of the long-term clinical data. And Aquablation is a receptive technique. It was demonstrated in the study that it removes as much tissue as TURP using transrectal ultrasound, assessing in the transrectal ultrasound. If you look at the PSA levels, which are our surrogate for prostate size, they were similar to TURP at one-year and two-year. Symptom improvement and flow rates we're similar to TURP at two-year as well. So, we would not anticipate any different or at long-term adverse events beyond the two-year period.

And then lastly, I'll talk on some of the clinical data. So we have the next slide up here. This is just looking at the guidelines that were referenced in the LCD. Just the

AUA Guidelines, all of these were published prior to or issued prior to the publication of our two-year RCT. We now have two-year data published as well as longer term data that we're gathering now.

Two comments I want to highlight is the AUA Guidelines were issued in 2018, after the prior version in 2010, but they were amended in 2019. And Aquablation was the only technology or surgical technology that was added to the guidelines, the EAU Guidelines in 2019.

The other point I want to clarify is the EAU requires a minimum of two-year clinical data which is why the recommendation is what it is and they will be reviewing our two-year clinical data in their current update.

And lastly, a reference in the LCD on the NICE guidance, we have special arrangements through the interventional procedures. There was a comment in the LCD that it's either designates a concern about safety or efficacy. NICE only had our six month data, but as you see in their publication, they noted that they no major adverse or no major safety risks that they were concerned with. So it was just the length of the follow up again, which they did not have two-year clinical data available.

Next slide.

In terms of the LCD, just to clarify a couple points that were referenced. The WATER study was a double blind study. So patients have been blinded after three years. Obviously, it's impossible to blind the operating surgeon. But in each one of our sites, we did have a blinded follow up team. So, every site had a blinded follow-up team that was separate from the operating surgeon to do that very point of remove that bias. So, while it's impossible to do the operating surgeon blinded we did have the blind follow-up team.

The Cochrane Review that was referenced, two things was they looked just strictly a randomized clinical studies. So failed to include our WATER II study, which was a single on study looking at large prostates. In addition, it was published prior to the availability of our two-year randomized clinical data.

And if you look at the database, there's actually similar sort of recommendations on other or comments on other BPH surgeries. And in fact, there is no Cochrane Review on TURP which is considered the gold standard today.

We would encourage the LCD to take a look at a recent publication of – in 2018 out of Germany that was a single center study at 118 patients. This longer term follow up is still coming but demonstrated early safety and efficacy similar to what was reported in the RCT.

And lastly the comment – there was a comment about the French study that the data was immature and remain weak. That was an introductory statements in the study was not reflective of the outcomes or conclusions of that study. And went on the next sentence, went on to say that there's a growing body of evidence supporting the efficacy.

Next slide, please.

I'll just touch on this AUA Guidelines. As I mentioned in 2019, were updated and you'll see there that they were the only surgical technology that was added was Aquablation. And as you look at it, the comment of level C evidence, you'll see that many of the other technologies or surgical approaches in the AUA Guidelines also have level C evidence and are covered by all or most of the Medicare contractors today. So the level of evidence have signed Aquablation is similar to many of the others that are being covered today, primarily driven by the length of the follow-up with the studies.

Next slide.

So, two primary studies we touched on the first one, the WATER study was the first FDA pivotal study randomized to the gold standard TURP. And again, it had an inclusion criteria, limitation of prostate size primarily because of the TURP arm and their limits on how large surgeons and the guidelines say to use TURP. Similar sort of inclusion criteria to many of the other BPH studies.

The conclusions from that study where Aquablation demonstrated a superior safety profile to TURP with comparable efficacy results in all prostates. In a subgroup analysis looking at the larger prostates within that study, it's demonstrated superior

safety and efficacy to TURP. And similar durable outcomes at two years, including retreatment rates, improvement in symptom scores, as well as peak flow rates, which is Qmax.

The second study, WATER II, was a large prostate study knowing that surgeons would want to use it on large prostates. And again, the only FDA prospective study completed for large prostate. The outcomes demonstrated statistically significant increase and symptom improvements that – at one year.

Safety and efficacy, similar to what we saw in the WATER study demonstrating that it normalizes. Normally as the prostate get larger and larger, they can get more complex from a surgical perspective.

And then lastly, the ability to take an inpatient procedure, many of these would be candidates for an open simple prostatectomy. Take that into the outpatient setting as 60 percent of these patients were done in the outpatient setting. And at one year, we have no retreatments.

Next slide, please.

So, a summary of some of the evidence and durability at two years. What you'll see here is kind of two groupings resective techniques, which include Aquablation, TURP, and green light lasers. Those are – TURP and green light are the majority of the resective techniques used today. You'll see on the right hand side here, the non-resective techniques which are UroLift and Rezum.

The patients included in these studies are very similar profile. So I think it's fair to look at them from a competitive perspective. What I highlight too on the bottom are the outcomes which are the primary efficacy advocacy outcomes for these technologies.

Two things to note, one is you clearly see difference in outcomes on symptom improvements or flow rates in resective versus non-resective and the impact of removing tissue.

The second thing to point is that if you look at the results in the Aquablation arm compared to TURP, either from the WATER study or from the GOLIATH, which is the landmark study for laser compared to TURP, you see very similar improvements

and symptom scores, improvements in flow rates and comparable retreatment rates at two years.

Next slide please.

Just kind of summarizing this, this is a published study from 2009, which listed 11,600 discharges, and it looks at the freedom from retreatment in TURP compared to laser, you'll see here this goes out to four years about an 8 percent retreatment rate in the TURP arm which is generally well accepted at about 2 percent per year, as you look at the laser arm higher at 12 percent. What I plotted here is the – you'll see the TURP from the WATER study. So the retreatment rates from the TURP on and the WATER study at one year and two year.

And then the Aquablation as well which is right in line and is a very linear progression in terms of retreatment rates for TURP. We do have some preliminary three year data from the WATER study, which shows no additional retreatments after two years and input 40 percent of the patients in and assuming that's what that last little shaded dots are represented. Assuming that holds out you'll see well within the linear results that we've seen in other published studies.

Next slide.

I just – on the WATER II study, about one thing to note this was a large prostate study the average prostate size was 107 grams which was two times besides the prostates included in the WATER study.

Next slide.

And in summary, that the WATER study results demonstrated very similar safety and efficacy to the WATER study, which was the smaller prostates. You'll note here that average length of stay was 1.6 days perioperative transfusion rate of 6 percent. And you'll see if you compare that to a large meta-analysis of open prostatectomy, which many of these patients would have been incurred, average length of stay of five days and transfusion rate of 24 percent. And this just compares it to other transurethral procedures and you can see that the outcomes are very encouraging.

Next slide.

Summarizes the challenges of using a transurethral approach for large prostates, what you look at TURP procedures that go longer than one hour and the resection time gets longer and longer as the prostates get bigger. Complications associated with transfusions T-U-R syndrome can be seen with laser. There's reported higher rates to retreatment that are seen, as well as long procedure times. Open prostatectomy cannot be done in the outpatient setting. Some of the new less invasive techniques that are not resective are actually contraindicated for prostates over 80 grams.

And HoLEP which is the other one that may be discussed is less than 5 percent of the procedures being done worldwide due to the learning curve. And you can see one of the consequences are a high rate of transient incontinence in those patients as part of that learning curve.

Next slide.

So in summary, you know, the technology been studied to the gold standard, demonstrating similar improvement symptoms and an efficacy. We, obviously a superior safety profile with a lower rate of sexual dysfunction and in large prostates, the opportunity to discharge patients quicker, provide a lower transfusion rate and a lower risk of complication compared to other technologies that are available today.

So in summary, next slide, please.

Actually, last slide here is the – these are just some of the sites that actually Aquablation and NGS and the number of claims have been submitted. So you'll see quite a few that are, despite the current non-coverage LCD that have adopted Aquablation and have systems placed in their institution. And we do have some claims that have been submitted as including a fee for service, as well as, Medicare Advantage.

Next slide.

So, again consistent with the other BPH procedures request coverage for the Aquablation category – the code 0421T, based on the clinical evidence, including the two-year clinical data demonstrating safety and efficacy comparable to other surgical techniques that are available, added to the AUA surgical guidelines. Medicare did

award new technology add on payments for the inpatient setting, demonstrating a substantial clinical improvement over existing treatment options, and then the ability to treat large prostates in an outpatient setting and very reproducible and regardless of the prostate size, unlike other transurethral approaches.

Thank you.

Carolyn Cunningham: Thank you. Dr. Haug, questions?

Craig Haug: I just have one question is there is – in process to get a category one code rather than T-code?

Matt Salkeld: Yes, we did that. We don't have the final results. We did have the –submit an application. The AUA submitted the application at the last time AMA CPT panel meeting. And we're waiting the final outcomes of that.

Craig Haug: Thank you.

Carolyn Cunningham: Any other one from the room or on the line?

Operator: As a reminder to ask a question or make a comment, you will need to press star one on your telephone. Again, that's star one.

Carolyn Cunningham: Thank you. Dr. Helfand?

Brian Helfand: All right. So we just ...

Carolyn Cunningham: Yes.

Craig Haug: We have to go back.

Brian Helfand: Yes, can we go back to the …

Carolyn Cunningham: We have to go back to Dr. Helfand, right?

Brian Helfand: So thank you guys again for the invitation to provide comments. I'm a urologist, I'm the Chief of Urology at NorthShore University. I'm a local Chicago guy, I did all my training and fellowship at Northwestern, and now I'm part of the University Chicago, up in NorthShore, so extended from Madison all the way to Wisconsin.

I am a consultant for a PROCEPT, the maker of Aquablation. Having said that is I'm not here on their behalf today, but rather to kind of share my experience. I have a high interest, both from a clinical standpoint and getting patients the right care, but also a large research interests also in why men not only get Benign Prostatic Hyperplasia or BPH, but also in kind of identifying obstruction into why they don't receive treatment. I have several NIH grants in this field.

Nonetheless, Aquablation has really met a lot of these needs. And just to give you guys some background here, most men as we age, our prostates grow, and this enlargement obstructs the bladder and makes it work harder to empty. And that is associated with a lot of lower urinary tract symptoms it's going to the bathroom frequency, frequently waking up in the middle of night, et cetera.

And this poses a large problem for a vast majority of men. In fact, if you query community dwelling men, over 85 percent of them will record some degree of urinary symptoms and or bother associated with the BPH or benign prostatic enlargement. And because of this, you would think that every man at some point should get treatment. Nonetheless, is the vast majority of men do not receive treatment in the United States and this is relatively related to many things, but because they do not like medications.

In fact, if you look at the overall compliance and use of medications for BPH, the vast majority over 60 to 70 percent will try it and within seven to 12 months, they will actually stop their therapies. And then they don't seek treatment and this is a very bothersome component that is, they're exhibiting avoidance behaviors meaning they will go places find bathrooms, say I will avoid going X number of miles without stopping on the golf cars – on the golf course, they will actually just use the bathroom there. So this is very bothersome.

So again, why are then more men not getting surgery? When you start querying men into why they avoid surgery, they – number one are afraid of undergoing an operation. Two they are afraid of long and dwelling catheters. And more importantly, as a lot of men don't like the perceived notion of sexual side effects. And when we talk about BPH and a lot of the conventional therapies, we're talking about retrograde ejaculation or decreased amount of ejaculate orgasm and affair that this is going to change their overall sexual quality.

So this is where my interest a while back started in Aquablation. And it's used for the treatment of BPH because it provided the opportunity for decreased side effects. And there's many reasons including the fact that the system doesn't use energy. It spares the anatomy toward part of the prostate, which is really responsible for the sexual function. And its overall when you look at the overall rate, it's about 5 percent in men undergoing Aquablation compared to the conventional therapies, which is 80 to 90 percent.

And when we talk about maintaining quality of life, this is important to most guys, which has not been offered by our gold standard, or any of the vast majority of therapies that are receptive and provide potentially long-term relief for patients. I showed this is really my initial experience with Aquablation. I have done many patients since then.

But I use these patients in particular, because these four were really coming to me not only with moderate to severe urinary tract symptoms, but they have been all maxed out on medical therapies. They really didn't like any of the therapies, never wanted to be in the traditional because of the sexual side effects. And they really were kind of wanting treatment but were definitely afraid of the other therapies. In fact, were putting and putting off these therapies and so they found the therapy what would have met all their needs.

And as you can see here, what we measure a patient's success in these type of treatments is by using the IPSS score. And that's just a measurement of how severe the urinary symptoms are. And if you look at the yellow boxes there, all of these men had severe urinary symptoms before and then after the procedure very quickly, they had significant improvements within their urinary symptoms.

But if you looked at all of these with the exception of one who ultimately became non-sexually active afterwards, not because of the therapy, but because they're so (expensive), all maintained the ability to have their (inaudible) normal sexual functions following. All were in the hospital for 24 hours and they all had significant improvements in their quality of life.

All were taken off of their medical therapies and all that well. And when we look specifically at the proxy for how much resection did we do, you can use PSA, which

is a commonly used screening test, blood test for prostate cancer. We can also use that as a proxy for a PSA volume. And if you look there was a significant reduction in the PSA and all of these patients which is equivalent to my series of TURP patients as well.

So this is providing and probably the level of evidence I need to reinforce that we are doing the adequate resection of tissue, and no adverse events were seen in these patients, but any of the patients are actually treated. And all of these, I should say, are real world experience that are comparable to the level one data that was provided by the Water I and II studies.

Next slide.

So, one of the really cool things that I like is that we can do this on men with really large prostates. And just so to understand this, when you do a TURP on a patient with a large prostate, just being there for hours and a lot of times you have to do that in two separate procedures. And then there's risk of complications of blood transfusions and other type of electrolyte of abnormalities that can occur.

So in more modern era, I do a lot of robotic surgery. I've historically done a lot of robotic prostatectomies to kind of remove the adenoma, the inner juicy part of the prostate as a treatment for these BPH patients.

That is a very costly procedure. The hospital stay is anywhere between three to five days. The bleeding is less compared to open procedures, and overall patients do well. But there is some complication risks that occurred because even though it's more minimally invasive, we are still opening the bladder and there's a lot of other, you know, potential leakage problems and infections that have since occurred.

But if you look at that compared to the Water II study and even compared to my own personal experience, Aquablation, kind of bypasses all of this. There's a limited amount of time we need to put a catheter. All my large patient prostates were decatheterized within 24 hours. They all – none of them in my study needed any type of transfusions.

We use minimal cutlery at best and simple traction occurred. And all again were discharged from the hospital within 24 hours. When you look at overall patient

satisfaction of my large prostate guides after Aquablation, they're equivalent if not better than the robotic simple experience that I've had. And so it's with that, but I really have been endorsing and using Aquablation.

And when I describe the overall choices that two patients of – we can do a TURP, we can do simple, we can do a laser depending on, you know, what your wishes are. I have yet to have a patient say I don't want Aquablation, and it's really motivated because of the decrease sexual side effects and the overall improvements. And, yes, while there's only limited to your database on when the technology came available, just based on the overall resection abilities of the Aquablation, there's no reason to think that these are going to have longer kind of occurrences.

Yet in fact to see a bladder neck contracture following this procedure, which historically, even after a TURP, or certainly a laser procedure was a big complication. So I am excited and certainly my patients have been excited to use Aquablation and certainly, especially in the Medicare community, do think that this will be the kind of standard for care as we move forward.

Carolyn Cunningham: Thank you.

Brian Helfand: Thank you.

Carolyn Cunningham: Questions to Dr. Haug?

Brian Helfand: Yes, I just have a couple. I think, Dr. Helfand, you were involved with the Water II study?

Craig Haug: I was not, actually. I was following along and I'm always one of the most cautious and certainly, that's what my colleagues would probably critique me as before I get involved in any type of technologies. If I'm going to offer it to a patient as a non-study therapy, but I want to make sure that the data is actually supported, and certainly, that was my motivation. So I actually held off.

Brian Helfand: OK, because I couldn't tell unless if you are part of the Water II, well, how many of the large prostates you've done. You alluded that you've done some. The first slide you had just showed (inaudible) under prostate. So it didn't show any of the large ones. How many large ones have you done?

Craig Haug: Now, about 10 to 12. So it's – you can still say it's a low number, but the large ones don't come around every day, so.

Brian Helfand: Do you think ultimately, the price for Aquablation will be mostly in the area of large prostates or equal for large and small?

Craig Haug: So it's interesting is that, you know, I think it certainly we'll have large size but really based on the overall profile, I think a lot of my men was smaller prostates, because of the decreased side effects are really kind of itching to get it. And again, is that because we're really conforming the Aquablation therapy to that size of the prostate, whether it's small or large, it really doesn't make a difference from a technical standpoint. And so that's really what I think is one of the most exciting parts about it.

Brian Helfand: Well, it's interesting you should mention that. My background is surgery. And you mentioned from a technical standpoint, and I read this, I couldn't – I mean, internists, always says if surgeons is just technicians, but it seems to me when I read this and see how automated it becomes, once it's programmed in, that this – that the "surgeon" really is in the role of the technician.

Do you have any – I mean, this doesn't say anything about the value of the procedure, just as one surgeon to another, that's what I – that was I myself thinking about. Any thoughts on that?

Craig Haug: Well, there's still – so as a urologist, you still need basic skills. And certainly, you know, there have been observers certainly from, you know, general surgery and other who've just been heard about this technology and kind of peek their head in. And you still really need to understand the ultrasound. How that – and, you know, and we're pretty well-verse in that just from doing biopsies and other prostate procedures. You still have to be somewhat savvy, if you will, in setting up, you know, cystoscope scope and aligning it appropriately and kind of defining the anatomy in there.

And yes, the actual, you know, technical part about it once it's all kind of primed and aligned, is that you can just, you know, press the button, but the technical skills on it are a little bit more.

And I only want to add to that is that we have a preliminary study that really, we, you know, have taken now about 20 of our trainees. And ask them to say, hey, I want you to take this ultrasound image if you're going to do Aquablation and plan out your resection plan.

And the cool part about it is that as a urologist, we all are pretty much can pick out the right plan to do and when we kind of draw ourselves, which really means that universally that we should have kind of uniform results when using this, which I can tell you for the other therapies is not there.

Brian Helfand: Thank you.

Carolyn Cunningham: Anyone else on the line or anyone here? OK.

Operator: As a reminder – as a reminder, to ask a question or make a comment, you would need to press star one on your telephone keypad. That's star one.

Carolyn Cunningham: Operator, while they're thinking about doing this which we see if Dr. (Kaplan) is connected.

Operator: What's the first name?

Carolyn Cunningham: Steve.

Male: He's in – I think he's in the operating room right now, so I'm not sure Dr. (Kaplan). I don't think he should be able to get on. (Inaudible).

Carolyn Cunningham: OK.

Male: Sorry.

Carolyn Cunningham: Never mind, Operator. We think (inaudible) where he is and he's not near the phone.

Operator: OK, thank you.

Carolyn Cunningham: OK. (Inaudible) on here.

Male: Excuse me on the speaker, we were informed perhaps incorrectly that we would only have 15 minutes total for presentation. Obviously, that is not the case. I really

prepared very abbreviated presentation because the time limitations and we would like to postpone if we could our response to the LCD because we think we understand now to present better information. This would not be the most comprehensive presentation because I only had – this whole had 15 minutes.

Additionally, we were told that this meeting would run from 12:00 to 1:30. And maybe that was incorrect as well. All of us have planes to catch, but I mean, I'll present if you want, but we really are requesting that we represent this at your next meeting. Is that possible?

Carolyn Cunningham: I think the issue is that would be – there probably will be another meeting until February, number one. Number two, we didn't anticipate as many presenters responding as they did, and I think we need Dr. (Inaudible) to present and then we'll (inaudible) the presentations.

Female: So what basically would have to happen is this is an open meeting for this LCD. So there's a process that's in line, right, that the comments period ends November 9th, and then it goes through the process of being formalized. So your best bet would be to present what you have and then submit in writing everything else that you wanted to submit because what I'm trying to say is, you can speak at – the meetings are scheduled for draft LCDs that are being brought to the meeting and this LCD will not be brought to the next meeting.

So commenting in February will not necessarily, you know, affect any of this. As far as the number of – the amount of time and the scheduling, it was at – in response to the responses, the last week of this time that we had open when we got most of the responses of people saying we would like to present and come.

And so, again, because of the nature of what this meeting is about, we had to accommodate them. And so we all scrambled, including me changing my flight just yesterday to accommodate and allow everybody to be listened to because that is what this meeting is for. But we couldn't really – we couldn't control that because we didn't get the request to present until, you know, the week of that it was going to end and we got several after it had been closed that we had to respond and say we're sorry, we can't accommodate you as a presenter.

So I do want to apologize as much as we can for the people that had the flights kind of issues, but …

Male: Is it possible just to take this off the table until February?

Female: I …

Carolyn Cunningham: We need to have a presentation at an open meeting.

Female: Yes.

Male: But could you hold off …

Female: That would mean the whole policy is not going through at all and has to start its whole, you know, the whole process all over again.

Female: And so we would like to request that.

Female: You know, we would have to probably take this offline for later on and see what's going on but it's scheduled to be presented at this meeting. So we will go ahead and do that.

Female: The two points is – we were told – based on your regulations that we have 10 minutes per presentation, and we prepared for 10 minutes.

Female: Per presentation.

Female: Right. And we were told that was for the whole company based on how we interpreted it. We were told 10 minutes for the whole company. So we were not fairly representative, point number one.

The second is there is a nor'easter happening. And if we don't get our flights, we will not be able to leave here.

Female: And so what I'm trying …

Carolyn Cunningham: The people would need to do is have Dr. (Inaudible) to do an introduction to the policy and then if you can present what you have, and if there's things that you need to present beyond that, we can look at it in writing or we can arrange it perhaps …

Female: (Inaudible) the presentation of what we could have been presenting. We could have had five or six speakers here.

Carolyn Cunningham: I don't want to spend any more time when talking about the presentation when we're wasting time as far as getting down what you have.

Female: I understand but I think we're not going to be fairly judged. That's (inaudible).

Carolyn Cunningham: Well, let us hear what you have after Dr. (Inaudible) speaks and then we'll see.

Female: OK. The next draft LCD is multi-marker serum test related to ovarian cancer testing. And as it says on the slide, serum-based tests have been proposed to triage patients with malignant versus benign adnexal masses. Suggested use of the test is to identify women who have a higher likelihood of malignant disease and may benefit from referral to a gynecologic oncology specialist. These tests are combinations of several separate lab tests known as MAAA and are performed on a blood sample by a reference lab using a proprietary algorithm.

Could you go to the next slide, please?

So this basically the summary of it is that this particular draft LCD is a non-coverage policy for multi-marker serum tests related to ovarian cancer testing for postmenopausal women.

Next slide, please.

So in the summary of evidence, we did a literature search in PubMed using the (Hayes) search criteria for each of the tests that we had looked at, which would be OVA1, OVERA, which is the next generation of OVA1 and the ROMA.

In total, we found 15 non-duplicated studies that were – for OVA1 and only six studies met inclusion criteria. Five of the six studies had limitations and that they included patients who had been evaluated by gynaecs prior to being tested, which is – which kind of negates the whole point. Most of the studies contained overlapping patient populations and all the studies were funded by the test manufacturer. There were five studies in all that we found that evaluated clinical validity.

Could you go to the next slide, please?

Medicare population is most likely to be postmenopausal women and according to evaluation and management of the adnexal masses, ACOG practice, bulletin number 174 which is November 2016, which replaced the one from 2007. The combination of an elevated CA 125 and a pelvic mass, ultrasound and a pelvic mass in the postmenopausal woman is highly suspicious of malignancy and patients with these findings should be referred to or treated in consultation with a gynaec.

In light of this, ordering and performing any of the lab tests that we reviewed in this document would be considered not medically reasonable or necessary for postmenopausal women and therefore is not covered. And after reviewing, we did have an open – we did have open CAC meeting, which is the Carrier Advisory Committee meeting in April of this year. And after that, we revise this to include a statement that claims for multi-marker serum tests related to ovarian cancer testing for premenopausal women may be considered for payment upon appeal.

So I think that is the last slide.

Charles Dunton: Thank you for allowing me to comment on the NGS proposed LCD concerning multi-markers serum test related to ovarian cancer detection. My name is Charles Dunton. I'm a gynecologic oncologist who's practice for 30 years.

Carolyn Cunningham: Can you hear – for the people on the phone?

Female: I hear it – I can hear it.

Male: I can, yes.

Carolyn Cunningham: OK, I was just concerned …

Charles Dunton: My financial disclosures are that I am employed by Vermillion and I'm giving this presentation on behalf of the company.

Next.

So what we are asking is that NGS recommend the coverage for OVA1, the multivariate index assay, as part of the evaluation of women with an indeterminate pelvic mass. This is after imaging is performed on a public mass. And it's not clearly benign or malignant. And in my experience, most ultrasounds which are the imaging

studies that we use fall into this risk. They're not benign – either clearly malignant or clearly benign, but the majority are in this indeterminate group.

Just to give you the current state of affairs of ovarian cancer, there's over 22,000 cases of ovarian cancer and it's most deadly gynecologic malignancy. Most cases are found in late stage disease with a higher mortality. And unfortunately, because of that, the overall mortality from this disease is greater than 50 percent. Most ovarian cancers are diagnosed with women over the age of 65. And while the majority of the pelvic masses in premenopausal – are seen in premenopausal women, the majority of the ovarian cancers are in postmenopausal women with masses.

Now there are approximately 1,000 gynecologic oncologists in the United States. And the difficulty is gynecologic oncologist – so I'm going to show you data that shows that they have the best outcomes when they treat women with ovarian cancer. But it is not possible for every patient with public mass to see a gynecologic oncologist. It's just not possible.

So the summary evidence we're going to support this, talk about FDA clearance, review published studies. We'll talk about national guidelines when Martin College of Obstetricians and Gynecologists give new data that we've just published on racial disparity in the detection of ovarian cancer and talk about coverage from other entities.

Next.

So FDA clearance in the Medicare coverage, if you look at OVA1, OVA1 has been cleared by the FDA for using – assessing risk of malignancy in a public mass prior to performing surgery and it is covered by Medicare by Novitas LCD. CA 125, however, is not cleared for assessing risk of malignancy. It's only cleared for following women with the diagnosis of ovarian cancer to see response to therapy or possible recurrence.

It is not covered by Medicare or a national coverage termination, specifically because it lacks the sensitivity and specificity of the test is not sufficient. And I have had patients where prior to my use of OVA1, I would order CA 125 preoperatively and the patient would call that Medicare would not cover that test which I thought was necessary, it will cover OVA1.

Peer reviewed evidence, which we will cite many other papers in our written replies, but OVA1 has been shown to have the highest sensitivity and negative predictive value when assessing the risk of an ovarian cancer with these undiagnosed and indeterminate pelvic masses. And this is very important for proper triage of patient prior to surgery.

So if you have a negative predictive value that's very high, that patient could be taken care of locally by your gynecologist and does not have to go to a gynecologic oncologist. And these papers that were cited here, it's important that this has the highest sensitivity for early stage ovarian cancer where we can do the most in taking care of that patient, properly staging them, and giving them better outcomes if they are taken care of by gynecologic oncologist. It's higher sensitivity in premenopausal women, also postmenopausal women as well and the sensitivity in non-Caucasian woman is something that is new that will show you the data on.

Next slide please.

So ACOG, the American College Obstetrician and Gynecologist, 2016, notes that OVA1 in conjunction with imaging shows high – negative predictive value as high as 99 percent when both studies are at low risk. And this allows for the general gynecologist to care for those patients and not refer them to a specialist.

OVA1 is not a diagnostic essay, but has to be combined with both clinical impression and imaging. OVA1 is far superior to CA 125. And I'll show you the data in detection of what we call less common ovarian histopathologies. So most ovarian cancers are high grade serious carcinomas. But about 20 to 30 percent are other mucinous tumors, endometrial tumors. And they are not – specifically CA 125 really targets only epithelium antigens, and OVA1 covers all of those histologies.

I use this table because of limitations of time, but I could show you many others. And what you see here is that the superior performance of OVA1 versus CA 125. Over 1000 patients have been studied prospectively to get FDA clearance and this is one of the trials. And if you look here at the non-ovarian histology, the sensitivity for OVA1 is about 80 percent. If you look at CA 125, no matter which cut-off you use is much lower.

And importantly, in early stage disease, overall, you see that – is that stage one disease is in the 80 percent. Stage two is 100 percent for OVA1. And in – with CA 125, it's in the 60 to 70 percent range. And if you look at premenopausal women in early stage, OVA1 is much higher sensitivity. And importantly, in postmenopausal women in early stage disease, you see it over 80 percent with OVA1 and 75 percent with CA 125 no matter which cut-off you use. And that's where we can do the most good in taking care of those patients and have the best outcomes for those patients by identifying them and getting them to the proper doctor.

Next.

And what is the influence of gynecologic oncologist? This is data that has been around for quite a while and why NTCN says that we should – that if you have a suspicion of ovarian cancer to go to gynecologic oncologist. If we're involved in the surgery and treatment, we properly stage the patient. We increase the chances of survivability and reduce repeat procedure. So the gynecologist takes care of a patient and finds that they have an ovarian cancer and they're not prepared to do the proper staging, including taking lymph node to sections performing an omentectomy, doing biopsies or even doing a debulking procedure, that patient probably have to go back for a second procedure.

Here's the data from showing that at least 10 percent increase survivability in patients taking care of by gynecologic oncologist. And some studies actually show an increase in survivability of up to 25 percent. And if you get the right – OVA1 allows us to get the right patients to the right doctor to improve overall outcomes.

Next.

So at the Open CAC meeting, I think we call it, one of the physicians said that, well, it's not a problem because all patients with a pelvic mass can go to a gynecologic oncologist. This position is from Connecticut. And if you look at the distribution of gynecologic oncologist throughout, this is from 2016, but I assure you that the numbers are not much higher, approximately 1000 gynecologic oncologists. And in Connecticut, that may be true, but in most parts of the country and in your coverage areas, it is not true. Women have to travel and there's a limited number of gynecologic oncologists.

Currently, I fill in for a physician in Southern Indiana, two hours – he's the only gynecologic oncologist within two hours of any other gynecologic oncologist. He's so busy. His waiting list is three weeks to see a patient and might be another three weeks before he operates on the patient. So get – by using OVA1 with a high negative predictive value, those patients that don't have cancer can be cared for and alleviate the burden on gynecologic oncologist. But it's really not possible for gynecologic oncologist to see every woman with a pelvic mass and perform the surgery.

Next.

ACOG recommendations for OVA1, so consultation to – or referral to a gynecologic oncologist is recommended for adnexal – woman with adnexal masses pre or postmenopausal with an elevated score on a formal risk assessment test, such as the multivariate analysis index essay OVA1.

Next.

And this is clinical care pathway that we think should be followed. So if an ultrasound is performed, which is a level ACOG recommendations, the only level A, and it's clearly benign that we watch and wait those patients. If it's clearly malignant, so we see ascites or masses outside of the ovary, we would – those patients should be referred directly to gyn-oncologist and just get a CA 125.

The majority of these are not clear. You're going to see complex masses. They may have some septations, some modularity, but it's not clear that they're cancer. And we think that this ACOG B level recommendation for OVA1 here will allow the patient to get to the right doctor and go to gyn-oncologist if necessary or if they're low risk patients be cared for by their general gynecologist.

Next slide, please.

So this is new data that we published just this year. And we looked at this because there were four independent publications outside of the company that looked at CA 125 levels in Caucasian and non-Caucasian, mostly African-American women. And they looked at levels of CA 125. And in each of those studies, where there were healthy women, women with family histories or genetic testing, putting them at risk

for ovarian cancer, or women with ovarian cancer, African-American women had lower CA 125 levels than Caucasian women. And we shouldn't be surprised about this, but we know the PSA levels are different between different ethnicities.

So we went back and looked at the perspective collected data within our studies and looked at the patients who were African-American versus Caucasian. And if you look at this data here, you see that the OVA1, the MIA is better in Caucasian women no matter what cut-off you use with sensitivity is about 90 percent. But in African-American women, while OVA1 is lower because CA 125 is part of the five proteins that we measure. It is a significantly better than CA 125 in this group of women.

So we feel this is a significant finding. I'm going to present this other gyn-oncologists, they say, we didn't know that. So we've just published this in the last several months.

Next slide please.

So payer coverage, government, Medicare covers this via the Novitas LCD and Medicare Advantage plans. Multiple Blue Cross Blue Shield plans to cover its testing across the country. Other commercial payers, such as Cigna covers this and it is in eviCore guidelines that OVA1 is a test that should be covered.

Next.

So in summary – and I could have presented a lot more data and we could have had more speakers here. The proposed LCD does not reflect publish evidence, in my opinion, clinical practice. I know you've excluded publications for OVA1, but we don't know which ones you've excluded because that (Hayes') data is not available publicly. We'd like to know why. We think it's inconsistent with ACOG guidelines for recommendations, which are national guidelines to follow. And it restricts coverage for postmenopausal women to CA 125. Certainly if the CA 125 is elevated in a postmenopausal woman with a mass, she should be referred.

The issue is what if it is not elevated, and you have a false negative CA 125? And we've shown you that sensitivity is better for OVA1. So, you may have a patients that you're saying, we want you to use CA 125 and they may have a cancer and they're not going to get to the right doctor.

And additionally, Medicare in their national coverage determination specifically excludes coverage of CA 125. And therefore, that's not going to be covered by patients who need testing.

And importantly, of the five components, we break out CA 125 in the result. So patient is not disadvantaged by not knowing what – the clinician is not disadvantaged by not knowing what the CA 125 is because that's given – a test score is given for OVA1 and the CA 125 is given out separately.

So I would like to ask Dr. (Randell) to come up and speak as a gynecologist who sees women with adnexal masses and has to make determinations of the best things to do for his patients.

(Dr. Randell): Thank you, Dr. Dunton. Good afternoon. Thank you for giving me the opportunity to really present my clinical experience as a practicing gynecological surgeon in Atlanta. I see a lot of women with adnexal masses and it really is a diagnostic dilemma for the practicing OB-GYN to know whether or not that adnexal mass is cancer or it's benign.

I remember taking my boards down the street, the Western Hotel back in 1997. And on my series of cases, I did a lot of laparoscopic surgery for adnexal masses. And back in 1997, that was like, oh my god, what is he doing? What if it was cancer?

Well, now, we have a better ability to know prior to getting the operating room, whether or not that adnexal mass is cancer. Because I'm not a gynecological oncologist, I'm a benign gynecologist doing a lot of surgery. And the worst thing that can happen for me is to get into a situation where I'm operating on a woman with an adnexal mass. And I don't know that it's cancer. Because what I could do is actually upstage her disease. And we know that if we can catch cancer at an early stage, there's a better prognosis.

So in terms of what the ACOG guidelines that were mentioned at the introduction, is that ACOG talks about women with an elevated CA 125 should be referred for surgery like gyn-oncologists. Well, the problem is, as you heard Dr. Dunton refer to is that 50 percent of early stage ovarian cancers have normal CA 125. I've had in my patients, several patients that have had ovarian masses. They had a normal CA 125, OVA1 was elevated, they were found to have cancer.

So had I taken that patient just rely on the CA 125 to surgery, believing that it was benign based on what ACOG is saying, I would have missed those patients. I would have potentially done a surgery that would upstaged her disease, and that would be a worst prognosis for the patient.

So I believe, especially with the postmenopausal patients, when we saw that – I don't know if we can go back to the slide there that shows the difference in sensitivity. We know that sensitivity is significantly increased in the postmenopausal patient with early stage disease. That's the challenge. Advanced stage disease is pretty obvious to anyone. It's the early stage disease that's difficult to detect.

And as you could see on that slide here, comparing CA 125 with OVA1 ...

Carolyn Cunningham: Next, you go back a little bit.

(Dr. Randell): Yes, one back (inaudible) disparity. Right here. So you can see here with the early stage, it says 91.7 percent sensitivity of OVA1 versus 75 percent for CA 125.

So, in clinical practice, you know, there's 1000 gyn-oncologists, there's about 40,000 OB-GYNs. So the majority of these women with adnexal masses are being seen by the general gynecologist. And we have to direct them to the oncologist. But the oncologist, there's a lot of work for them. They don't have time to be managing benign disease.

So with a high negative predictive value of OVA1, we can keep these patients. We talked about the improved sensitivity, but negative predictive value is key as well that is if a patient has an adnexal mass and she has a low risk score on OVA1, she's unlikely to have ovarian cancer. That patient could be kept by the general gynecologist and operated on, and not worry about cancer.

So with OVA1, we've seen improvement in sensitivity. That's the ability of the test to detect the disease, that being ovarian cancer, as well as the improved negative predictive value.

I like to call that peace of mind, peace of mind to me as a practitioner and peace of mind to my patients saying that you have a mass, but with the OVA1 score showing low probability malignancy, it's unlikely this is cancer. And that is very powerful to a

patient to know prior to go to the operating room that it's unlikely that she has ovarian cancer. Thank you.

Female: I actually had a question.

(Dr. Randell): OK. To me or Dr. Dunton?

Female: To you. You know, you mentioned something now and Dr. (Shiro) had also mentioned this during the CAC, which was both of you gave examples now that technically with what you had described earlier, this person would not be getting OVA1 in the first place because the ultrasounds was, you know, you were pretty sure about the ultrasound and …

(Dr. Randell): No, it was indeterminate. So it's indeterminate. If it's obvious cancer, there's really no need to do any additional testing. So if I see ascites, if I see bilaterality, if I see large masses with (inaudible), it's high probability of cancer, that patient would probably referred – there would be no reason for me to not ...

Female: You just said that you would have gone ahead and done that or not you, but the patient would have gone ahead and had surgery and it would have been exposed, right? It would have been – it would have worsened her situation or elevated her situation. But by doing OVA1, she ended up getting to have the surgery via radiation by a gynecologic oncologist.

So unless I'm mishearing what you said, so therefore something was abated – avoided and I'm just bringing that up because that's the second kind of time that when it's time to give an example, the examples we're getting are people who had I not done this, you know, like the patient's presentation or picture look like it was OK, right?

(Dr. Randell): So let me clarify. The scenario would be the patient who had an indeterminate mass. So we know there's a mass but doesn't meet the criteria for what we consider to be a malignancy. So we're not sure what it is. So when we do additional testing, most OB-GYN may choose to do CA 125. If the CA 125 is elevated in that indeterminate mass, according to ACOG, that patient would be referred to the gyn-oncologist.

So what I'm saying is that for the early stage disease, we have indeterminate mass and she's one of the 50 percent of women with early stage disease abnormal CA

125. She would not be identified. She would then be offered it on perhaps by a benign gynecologist like myself. If that patient that had an indeterminate mass in ultrasound has a normal CA 125, we failed to detect …

Female: But would that mass indeed be identified as indeterminate had she been early or would have – would have mistakenly been identified as nothing?

(Dr. Randell): And that's a good point. That's – that deals with the subjectivity of ultrasound. Because remember, it starts off with a ultrasound. We do the ultrasound and we identify the mass. At that point, we need to decide, is that a benign mass or malignant mass? What do we have to do that? OVA1 helps us to decide that. If the ultrasound criteria is such that it's obviously a cancer, we can send that patient right to the gyn-oncologist without any additional evaluation.

What OVA1 does is it helps me clarify those patients as indeterminate masses on my transvaginal ultrasound …

Female: So you're basically saying if you cannot say it's definitely cancer, it's indeterminate.

(Dr. Randell): Right. It doesn't meet certain criteria on ultrasound – ultrasound features, then OVA1 would be that test and help me decide if it's benign or malignant. If the OVA1 score has a high probability of malignancy, that patient who had an indeterminate mass on ultrasound would then be referred to the gyn-oncologist. Because right now, if you look at ACOG statement, ACOG guidelines, it specifically talks about an elevated CA 125.

The problem is, is that 50 percent of women with advanced stage – I'm sorry, early stage ovarian cancers have a normal CA 125. OVA1 finds those women where CA 125 misses. So that's the whole idea about OVA1 being more sensitive. It's finding more disease. And with the negative predictive value, telling a woman that she has a negative or low probability score on OVA1, I can take that to the bank, I can tell you with almost 99 percent certainty that you do not have an ovarian cancer.

But with a CA 125 only being 50 percent, I'm right and I'm wrong equally. I could flip a coin rather than even ordering blood tests. And so negative predictive value for CA 125 in this situation is 50 percent, right? So the reassurance that I have that the mass negative is in the high 90 – 99 percentile. So improves sensitivity of detection.

And again, we're talking about those indeterminate masses. If you do an ultrasound and clearly has features suggesting ovarian cancer, that patient should be referred to the gyn-oncologist. I'm not looking for a reason to keep her in my practice. I would refer her out.

But if I have a patient who has an early – a patient has an ultrasound that's indeterminate, and I now add OVA1 and I have a high probability score, that patient is now going to get referred to the gyn-oncologist. And we see that based on the sensitivity that you're going to find more patients with ovarian cancer in the early stage cancers with OVA1 compared to CA 125.

Male: (Inaudible).

(Dr. Randell): Thank you.

Carolyn Cunningham: Operator, in the meantime, could you be finding Dr. (Schulman)?

Male: Yes, he is a ...

Female: Dr. (Schulman) wants to call in but he can't get into the toll free numbers, they're a direct line. I can put them on my cell phone because he's out of country.

Carolyn Cunningham: You can put him in my cellphone if you want.

Female: On your cellphone?

(Inaudible)

Female: There’s going to be a (text) in your cellphone.

Charles Dunton: Can I explain again on the clinical pathway if we can get to that slide? Try to clarify it.

Female: Forward or backward?

Charles Dunton: I think it is …

Male: Forward.

Female: Forward. OK. Could we …

Female: 590-317.

Charles Dunton: One more, one more, one more.

(Inaudible)

Charles Dunton: So as I said, if you have a simple cyst on ultrasound, you won't do anything about that. You wouldn't even order a blood test. You might repeat the ultrasound to make sure that it doesn't grow. But that is sort of the clearly benign reason.

Then if you see patients with, you know, projections into the ovary complex masses, ascites or disease outside of the ovary, that's going to be considered clearly malignant. But most of these ultrasounds come in as not clear or indeterminate. They say, well, we think that this could be something but we're not sure. And so that can be a low risk one but it can be harboring a cancer.

So CA 125 does not give you the negative predictive value you want as a benign gynecologist, Dr. (Randell) said. You would want to have a very high negative predictive value that can reassure that you can take care of that patient. And if the score is abnormal and normal CA 125, you would say let's send this person to the gyn-oncologist.

(Dr. Randell): It clears up the diagnostic dilemma for the gynecologist who've seeing these patients. And as I say that relying on CA 125 is unreliable, just based on the intrinsic low sensitivity of CA 125 especially in the premenopausal.

(Steve): Hello? Hello?

Male: Steve?

(Steve): Yes.

Male: I can hear you. I can't hear anything else.

(Steve): I know. At least you're here. Yes.

Operator: Yes, this is the conference operator. The speaker's line dropped.

Male: Oh, can that be undropped?

Operator: If she redials back in …

Male: Rats. OK.

Female: All right, if someone can chat her, she may not know.

Male: Let's see if I can …

Female: I sent a text to (Ola).

Male: OK.

Male: OK.

Male: Thank you.

Carolyn Cunningham: Are we back?

Operator: You are now connected.

Female: I am here Carolyn.

Carolyn Cunningham: OK, good. We apologize for the disconnection. We don't know how it happened, but it did. We're glad you're back. Does anybody on the phone have questions or comments for the last three presenters?

(Inaudible)

Female: Did they hear Dr. (Schulman)?

Female: Did you hear Dr. (Schulman)?

Female: No, no, we didn't.

Operator: Your line dropped off right at 4:00 Eastern Time. So anything before that, no one heard.

Male: Anything after that, yes.

Operator: After that, sorry about that.

Carolyn Cunningham: Who was speaking at 4:00?

Female: Well, he was the one speaking.

(Inaudible)

Female: Yes, just five minutes ago. So he was the one speaking, the last – the last speaker was the one speaking. So you didn't hear him at all?

Male: No, I think you were in the process, Carolyn, of getting somebody else on your phone or something. We didn't hear that person.

Carolyn Cunningham: So the last person who spoke particularly about CA 125 and is out of the country?

Male: I don't think so, no.

Female: Do you want him to get back on the phone?

Carolyn Cunningham: I think what we'll do, is looking at the audience here, I don't know who was on the phone, we'll arrange a time that he can be on the phone with the staff at NGS.

Female: OK.

Female: And he can call in to us (anytime possible).

Female: OK.

Carolyn Cunningham: Any other questions or comments on the phone or here?

Well, I want to thank everybody for your patience and your endurance. We appreciate the interest in the fall season. That is a lot of (good) information. So thank you very much.

Male: Thanks.

Carolyn Cunningham: Anything that – anybody on the phone has to add?

OK, thank you.

Male: Thank you.

Operator: Ladies and gentlemen, this concludes today's conference call. Thank you for participating. You may know disconnect.

END