National Government Services, Inc.

Moderator: Dr. Ola Awodele

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Coordinator: Welcome, everyone, and thank you for standing by. I would like to advise you that today's call is being recorded. If you have any objections, you may disconnect at this time.

All participants will be in listen-only mode until the comment sessions of today's call. I would now like to turn the conference over to (Ola Awodele). Thank you so much. You may begin.

Dr. Awodele: Thank you. I would like to welcome everybody, good afternoon to the draft policy meeting for national government services J6 JK June open meeting.

So thank you everyone for signing on. And at this meeting we will be presenting about four draft LCDs and I'm so excited, we're so excited because we have four speakers presenting at this meeting today.

I'd like to remind everybody that as we present the draft LCDs, there will be opportunity for people to give their comments, their oral comments. And just to remind you that you could also send in your comments in writing to us at partblcdcomments@anthem.com.

So we will proceed now with the meeting and we'll continue to give you this email throughout the meeting. And I'm doing this introduction on behalf of all my co-medical directors who can see on your screen. Next slide please.

Okay, so the proposed LCDs for today is Drugs and Biological, there's also DL39297 which is the off-label use of rituximab and rituximab biosimilars. There's DL39314 which is off-label use of intravenous immunoglobulin, IVIG. And last but not least there's DL37733 biomarker testing for prostate cancer diagnosis.

Next slide please. Okay, so I'm going to start off with this - the first draft LCD and I just want people on the call to know that this draft LCD is actually a revision of a currently existing LCD titled Drugs and Biologicals.

For those of you who are familiar with our Drugs and Biologicals LCD, it's somewhat of an umbrella LCD where we list and remind the public of the various IOM and policy manual references concerning drugs and chemotherapy drugs and biologicals and then we have articles attached to this policy for different drugs.

We are - because of the fact that just through the IOM, off-label uses are covered for medically accepted indications as defined in 100-2 Chapter 15 Section 50.4.5. We are revising this LCD to remove billing and coding for nivolumab, to remove billing and coding for infliximab and biosimilars.

And this is because it's very well established within the manual that off-label uses that are noted in the compendia that has been approved by Medicare are stuff that

is automatically covered so we don't feel that we need to have an article out there further saying this - stating this.

So this is only coming to the open meeting just to let people know that we are removing the billing and coding, nivolumab and infliximab and biosimilars. Next slide.

And they're also going to be removing and transitioning to individual proposed off-label coverage LCDs, the other two that we're going to be discussing going forward which would be the rituximab, and rituximab biosimilars and the use of intravenous immunoglobulin or IVIG.

Next slide please. Okay, before we go to off-label use of rituximab and rituximab biosimilars, although I'm not really expecting much by way of comments, this is something that we do after every LCD or draft LCD that we propose so I will pause at this moment and ask that the operator open the line of anybody who has a comment for the revised LCD.

Coordinator: Absolutely. If you would like to make a comment at this time, please press star 1 on your phone. Be sure your line is unmuted and record your name so you may be introduced. Again to make a comment, please press star 1.

It may take just a few moments for them to come through. Please stand by. I am showing no comments at this time. But I will continue to monitor.

Dr. Awodele: Okay, thank you. I wasn't really expecting any. So we'll go on to the next draft LCD for this meeting and it's the off-label use of rituximab and rituximab biosimilars. This is a new draft and this new policy addresses the off-label use of rituximab for non-antineoplastic conditions.

The use of rituximab for label indications is covered and not addressed in this policy and I want to stop and say that off-label in the cases of these draft LCDs then going forward as we rolled them out when it comes to drugs means that it's not per FDA approval or per label and it's not in any of the approved Medicare compendia.

So in the IOM we have the ability or we have the instruction that we can review and on individual reconsideration, we can pay certain claims but as per what LCDs are, if we notice that, yes, we are paying a lot of these and it - you know, the literature and everything is moving towards this being a widely used off-label use of the drug, then we will create LCDs that let people know that this is what NGS or National Government Services has reviewed and feels is okay to use this drug.

I also want to note that there is always going to be the claim appeals process and the ability to reconsider the LCD going forward to ask that other indications be added obviously following reconsideration rules there. So off-label use for antineoplastic therapy is not addressed in this policy at all.

Next slide please. So here are the off-label uses of rituximab and rituximab biosimilars that we have considered after reviewing to include in this LCD, remembering our definition of off-label in the case of these drafts.

So it includes acquired hemophilia, thrombotic thrombocytopenic purpura, multiple sclerosis, idiopathic inflammatory myopathy, immune-mediated myopathies, immunoglobulin G4-related disease or IgG-4 RD, antibody-mediated rejected, immune thrombocytopenic purpura or ITP, chronic inflammatory demyelinating polyneuropathy or CIDP. And actually, this particular diagnosis is the reason was sent

in, we got a reconsideration request sent in reconsidering our drugs and biologics LCD asking that these diagnoses be added to the - what was then the article for rituximab and that's what spurred the review of this article and the creation of this LCD and Sjögren's syndrome and systemic sclerosis.

Next slide please. Of note in our review and in our research, we found a few diagnoses that we thought were considered investigational that we also included in this LCD and those would be Behcet's syndrome, cerebral ataxia and polyarteritis nodosa.

And so that's really what I have to say about this draft and we don't have any presenters for this particular draft but I would like at this time operator if we can open the lines for any comments.

Coordinator: Again, if you would like to make a comment at this time, please press star 1 on your phone and be sure your line is unmuted. Again it's star 1 for any comments. I'm still showing no comments at this time. You may proceed.

Dr. Awodele: Okay, thank you. So we'll go over it. We'll consider this draft closed and as I said earlier, comments are always welcome in writing. The next draft LCD is, if you can go to the next slide, thank you, is the off-label use of intravenous immunoglobulin IVIG.

Again, this is a new draft and this LCD defines off-label uses for IVIG that are non-FDA approved indication and for the purpose of this policy, those indications also not listed as covered by major drug compendia.

IVIG is a blood product containing human immunoglobulin specifically prepared for our intravenous infusion.

IVIG is used in the treatment of primary immunodeficiency diseases, featuring low or dysfunctional antibody levels to prevent infection and for certain inflammatory autoimmune and other diseases featuring to interfere with harmful antibodies and for blocking damage from immune cells. Next slide please.

So upon review and in our research, here are the off-label uses of IVIG that we consider covered according to this draft LCD and that was the stiff-person syndrome, autoimmune retinopathy, pure red cell aplasia related to human parvovirus B19 infection, hematopoietic stem cell transplantation, Chronic Graft versus Host disease, systemic lupus erythematosus, scleromyxedema, systemic capillary leak syndrome or Clarkson's disease.

Next slide please. So for this particular draft LCD, we did get a request to speak at this open meeting. Dr. Vradii. Operator, if you could open up Dr. Vradii's line so that she can begin her presentation. And we'd like to thank you very much, Dr. Vradii, for doing this.

Dr. Vradii: Hello. Can somebody hear me?

Dr. Awodele: Yes, I can hear you.

Dr. Vradii: Okay, excellent. Well, hello everyone, and I truly appreciate this opportunity to present to the panel. I am a rheumatologist in one of the small hospitals in Brunswick Maine.

And as you know in rheumatology we have quite a few conditions that we struggle with and we certainly need additional treatment options. And just in the last few

slides you mentioned a few diseases that are in the field of rheumatology and require additional authorization of certain medications including rituximab.

And I would like to talk about IVIG for actually use of systemic sclerosis which was not on previous slide and I'm not exactly sure who we have included in today's panel, so I will try to give a brief overview of the disease so that the panel understands the clinical difficulties from the physician standpoint which we struggled with on a daily basis.

So if I could have next slide please. And I do not have anything to disclose. I have no affiliations with any companies and nobody approached me whatsoever.

I am doing this purely for my patients and to tell you the truth, I have lost patients to this devastating disease and I am trying to offer patients some treatment options that may or may not work for them but I would like to have them available as options.

Next slide please. So systemic sclerosis is the correct terminology of the condition I will talk about, but the simplicity of it I will refer to it as scleroderma, and some people may know it as a condition that is manifested by hard skin.

Next slide please. So to get to the basics of the disease, the bottom line of the pathogenesis in scleroderma is over production of scar tissue by fibroblasts. However, there are certain other pathways that I implicated that lead to hardening of tissues in different systems of our body.

So in the first picture on the left, you see - actually first two pictures, you see involvement of skin and it doesn't only involve the skin, it involves vascular system as well and you see symptoms of Raynaud's on the left.

Second picture is showing symptoms and findings of tissue damage or actually necrosis of fingertips due to insufficiency of blood flow and this gangrene or necrosis can extend and frequently patients lose digits due to this disease.

On the third picture you can see the disease affecting skin, on the face, but it can affect skin on the entire body. The fourth picture shows you the arm and I am sure you cannot probably appreciate the abnormalities on this picture but I will give you an example for example with the degree of tightness of the skin on this arm.

A person for example may not be able to flex the elbow and these patients come in to me with inability to care for themselves. They can't bend their arms and comb their hair or brush their teeth or, you know, put their pants on. So significant disability.

The next slide is showing a few other pictures that, you know, shows involvement of arthritis, involvement of GI system and skin essentially anywhere on the body.

Next slide please. In addition to the visual symptoms, we can assess it affects lungs, it affects heart, and it affects GI system. Next slide please.

So this is an example of how a normal skin would be able to pinch and how a sclerotic or very hard indurated skin is unable to be pinched due to severe thickness or tightness of it.

Imagine your skin have been hard like a scar tissue although it's affecting your entire skin. Some patients present themselves as feeling being encased in something very tight or they call themselves as tin men. Next slide please.

So this is another complication, an array of complications in hands and extremities but most commonly in hands with severe flexion contractions in the top left figure and then skin sclerosis, digital sclerosis due to blood vessel involvement.

Next slide please. So what do we have for treatment options for these patients? It depends on manifestations each patient presents with. Some patients have mild manifestations and we are able to treat them symptomatically. However, when patients present with significant lung involvement or GI involvement, our treatment options are quite limited.

Next slide please. So this slide is showing a variety of system involvement and treatment options that we have. While skin involvement can lead to skin necrosis and digital amputation, it rarely does so and we have some treatment options.

However, when similar process occurs in GI tract, these patients are at very high rate of essentially morbidity and mortality from gastrointestinal involvement.

Imagine that your entire tract is essentially a scar tissue. It is not moving. It is not absorbing nutrients. So these patients have a very stiff esophagus, very stiff stomach and inability to absorb nutrients through their small bowel.

In addition to significant nutritional deficiency that they develop, significant weight loss that they develop, they also develop secondary complications due to significant heartburn because of the esophageal involvement. And these patients have frequently aspiration pneumonia or secondary pulmonary manifestations as a result of CBA gastrointestinal manifestation.

So if you would think what can we help these patients whose GI tract is essentially a stiff pipe that has been losing its function and the short answer, we do not have treatment options.

Some of the treatments we use for lung disease do not usually show efficacy for GI involvement. And while we use PPIs and prokinetics and rifaximin and a few other options that we can offer with symptomatic management, we lack definitive to any other treatment options in fact with GI involvement .

So once a person has GI manifestations of systemic sclerosis, in my personal experience, they would usually die anywhere from three months to 12 months after the diagnosis.

There are some - next slide please. So these are some of the treatment options I used. We have for persistent GERD and usually they're, you know, quite limited. Next slide please.

o fortunately, we have some literature that has some case series, very small trials. Some of them including 15 patients, some of them including 46 patients of use of IVIG in systemic sclerosis. And while we know how IVIG or what the mechanism of IVIG is, we do not clearly understand how it works in certain autoimmune conditions.

However, in systemic sclerosis, the hypothesis is that by regulating T-cell proliferation may control this uncontrollable fibrosis that occurs in scleroderma. Next slide please.

So IVIG in addition to its immunomodulatory actions, neutralizes other auto-antibodies that promote auto- inflation and different conditions including systemic sclerosis. And there are a couple of proposed mechanisms that have been hypothesized that may be having a role in systemic sclerosis.

This treatment was shown to be safe when used for other conditions, and due to lack of significant known side effects and no other available options to these complication of systemic sclerosis, these may be potentially an option we could offer our patients.

Next slide please. So systemic sclerosis, and actually quite a few other rheumatic diseases are not frequent diseases. They occur, you know, very occasionally but when they do, these patients can become very sick and may potentially die as a result of complications.

Yes, we do need many other treatment options. As you mentioned rituximab has been explored for systemic sclerosis as well but there is some data supporting use of IVIG specifically for GI involvement of systemic sclerosis and I'm hopeful that in the next few years, we'll have more data to support its use.

I appreciate panel for paying attention to this important matter that I struggle with in my daily practice and I hope that you will consider this, including systemic sclerosis for off-label use of IVIG in your LCD as well. Thank you so much and I will take any questions.

Dr. Awodele: Thank you, Dr. Vradii. You know, as you noted also, we also saw that when we were reviewing in terms of these paucity of documentation that's out there. But I thank you for your presentation and I don't really have anything to add or say about, you know, this in terms of being against it or being for it.

However, I do also want to just encourage you that remember there's always the review process, you know, the appeals process for any of these - the claims, claims in general.

And so we appreciate you presenting and we appreciate everything that you do for patients and the concern and love you have for your patients. So I would - I think you did submit this to us. If you would...

Dr. Vradii: Great. Thank you so much.

Dr. Awodele: Great to have a copy of your presentation before. So thank you very much, Dr. Vradii.

Dr. Vradii: Yes, yes. Thank you.

Dr. Awodele: So, operator, I'd like to open this policy, this draft policy to the public for comments, please.

Coordinator: Absolutely. Again, if you would like to make a comment at this time, please press star 1 on your phone and record your name so that you may be introduced. Again that's star 1 for any comments.

I will continue to monitor but I'm showing no comments at this time.

Dr. Awodele: Okay, thank you, operator. I'd like to remind everybody that the email address to send in any comments in writing is partblcdcomments@anthem.com. And this email can be found at the bottom of any of the draft LCDs that we have that we're presenting today. So thank you.

Let's go to the next slide please. Okay, so I'm going to hand over to Dr. Noel for the next draft LCD. Dr. Noel?

Dr. Noel: Thank you. The next draft is DL37733, biomarker testing for prostate cancer diagnosis revised. These changes were based on a reconsideration request on this topic and

the coverage criteria has been revised to allow limited post op coverage and limited repeat testing coverage.

The provision of limited coverage for biomarker testing for prostate cancer diagnosis has the potential to not only decrease the biopsies and the associated risk, but also reducing detection of indolent disease and the attendant risk of over treatment.

The primary aim is to increase specificity compared with PSA without decreasing the sensitivity to diagnose high risk prostate cancer. Next slide please.

Given the state of flux of PSA screening in general, combined with arguably tentative and in some ways diminished guideline support secondary to the almost complete absence of level one or outcome studies and the adjunctive biomarker testing, NGS will provide very circumscribed coverage.

Coverage will be limited to patients with moderately elevated PSA level, but with no other, even relative, indication for or against biopsy largely based on NCCN guidelines.

These are men for whom the decision about whether to proceed with prostate biopsy is most ambiguous, and therefore for whom the information is most likely to impact clinical decision making.

Criteria for the EPI test are somewhat more liberal than the RCT patient mix and results. Nevertheless, none of these assays are recommended for routine use as they have been, excuse me, as they have not been prospectively tested or shown to improve long term outcomes such as quality of life, need for treatment, or survival.

Next slide. While the result of mostly industry-sponsored validation studies are promising, benefits remain theoretical, namely, that fewer biopsies of men with moderately elevated PSA is inherently a good thing.

Certainly it is good in the short term for men to avoid an unnecessary prostate biopsy. Not good, however, are necessary biopsies missed due to false negatives. Moreover, even the definition of unnecessary may be evolving.

Also some studies overrepresented men for whom the information is less likely to be helpful, those with positive digital rectal exam, PSA levels outside the (gray zone) or older men not candidates for surgery, or underrepresented others, such as high-risk groups such as African American.

Comparative studies of the many biomarkers are lacking and it is unclear how to use the tests in practice, particularly when test results are contradictory. For all of these reasons, the long-term benefit of these tests to net health outcome is not yet clear.

Next slide. We have three speakers for this draft. We will start with the first speaker. It is Dr. Johan Skog. Dr. Skog, please proceed.

Dr. Skog: Thank you so much. Can you hear me?

Dr. Noel: Yes, I can.

Dr. Skog: Great. First of all, thank you so much for allowing me the opportunity to present here to the panel.

So if you go to the next slide, so my disclosures is that I am the Chief Scientific Officer, Vice President of Exosome Diagnostics, a subsidiary of Bio-Techne. Next.

So just to sort of set the stage, we do strongly support this proposal to the - for biomarker testing because we do see that it will expand to Medicare access to biomarker testing for prostate cancer which we feel is very important. And we do think that LCD reflects the validation studies and the NCCN team guidelines for our assay, the ExoDx prostate test EPI in short.

But however, we do recommend two modifications to the proposed LCD that are consistent with scientific evidence and clinical practice and those would be to remove the exclusion for patients with an abnormal (DRE), as well as allowing the test order by the treating physician other than neurologist or oncologist. Next.

So for the benefit of the panel here, I intend to just go over briefly what the ExoDx EPI test is. So this is a urine-based liquid biopsy test that doesn't require digital rectal exam or prostate massage prior to the capture of the sample. So the test can actually be done in the urologist office or even at home after the urologist have ordered the test.

And it's intended for men 50 years of age and older with a PSA in the 2 to 10 nanogram per milliliter range which is also considered that the PSA gray zone because men with a PSA from 2 to 10 are especially challenging when determining the decision to biopsy because that is really the range where PSA performs poorly.

The test is performed in our CAP/CLIA lab in Waltham, Massachusetts. And this test has been included in the NCCN guidelines for prostate cancer early detection since 2019.

Next slide. Over the years, we have produced quite a significant number of publications and evidence for the use of the EPI test. We've done, not only one validation of our cut point, but also actually two prospective validation of our cut point as well as a clinical utility study that has a very novel design with a blinded control arm which we believe qualifies for a level one evidence and we also have support publications and other aspects, none with a prior negative biopsy. .

And we've also shown that when the biopsy result is wrong which is unfortunately often is, the EPI test actually correlates to the radical prospecting outcome-based pathology even when the initial biopsy result was erroneous.

Next slide. So we - the EPI test gives you a score from 0 to 100. However, we have a validated cut point of 15.6 which - where the specifications are listed in the upper left corner here where the sensitivity and negative predictive value are over 90%.

And we've done a pooled analysis of all our validation trials and that has generated this nice graph in the lower left corner that shows you that with an increasing EPI score, there is a higher chance of detecting high grade prostate cancer upon a 12-core TRUS biopsy.

As you see it's increasing up to about 50% so when you have an EPI score, there is about 50% chance of finding high grade prostate cancer from the biopsy.

An important to note here is that biopsy can actually miss high grade prostate cancer in up to 50% of the cases so there is no possibility to have a near perfect correlation up to 100% when that goal is biopsy.

So how is the test really used by the clinician? So in the upper right corner you can see an example where you have three patients that are all in the intended use population.

And based on the age on the PSA level here, there is no way for the urologist to really differentiate between the risk of having high grade prostate counts among these three patients because all the standard of care parameters here are near identical and have here identical risk.

However, the EPI prostate test is giving you an additional data point that is not dependent on any of the standard of care parameters. So it's a completely new information with the genetic targets that, you know, have in the EPI test and that gives you an additional information for how you should - who you should biopsy.

And in our clinical utility study with a blind control arm, we found that urologist with access to the EPI test found 30% more high grade prostate cancer compared to the blinded control arm that used standard of care alone. And patients with a negative EPI score underwent less biopsies as shown in that study.

Next slide. So the first recommendation is to remove the suspicious DRE limitation. The EPI published data consistently demonstrates utility in patients with suspicious DRE and in all our validation studies we have patients with suspicious DRE included.

So our performance metrics include these patients and the pooled analysis from all our validation trials includes 155 patients with suspicious DRE and there is no significant difference in EPI performance in this population.

And as well the NCCN guidelines inclusion of EPI is not limited to patients without DRE suspicious for cancer. And the DRE is acknowledged to have very strong limitations and some clinicians actually advocate against the use of DRE as a single sort of biomarker entity here.

Next slide. The other recommendation is the removal of limitation to order the test only by urologist or oncologist and the reason for this is that we also want to include physicians that actively manage or refer prostate cancer patients to the urologist because urologists want the referral PCP network also to be able to order the test and this also increases deficiency on the urologist's office and leads to a quicker decision process with fewer urologist visits.

And there are some challenges in some geographies, limited access to urologists, oncologists. Next slide.

To summary, to conclude, we do strongly support the expanded use in this proposed LCD. However, we do okay recommend the additional changes in their final LCD specific to EPI which includes the removal of the DRE limitation, the removal of the limitation of urologists, oncologists ordering the tests. And thank you for that.

Dr. Noel: I want to thank you for your presentation. Please send in your written comments for us to use in the response to comments document and to take a look at the draft as it is in its present form to see if we need to make any changes.

The next presenter is Dr. David Albala. Go ahead, Dr. Albala and give us your presentation.

Dr. Albala: Great. Well thank you very much and I hope you can hear me fine and what I'd like to do over the next few minutes is talk to you as a practicing urologist. I've been a urologist for 33 years. I spent 21 years in academic medicine, both in Loyola University and Duke University. And now I'm in a private group of 33 urologists in Syracuse, New York.

So if we could go to next slide, my practice has over the years evolved. If somebody could change the slide. My practice over the years has evolved into seeing significant number of prostate cancer patients.

When I was at Duke, I developed a robotic program at Duke for prostate cancer and was doing about 300 prostatectomies a year. When I came to Syracuse, that number dropped and the numbers have dropped a little bit due to active surveillance and also the preventative task force recommendation of not doing PSA testing.

So we've seen a drop in the number of surgeries and also the identification of patients with prostate cancer. And I think over the years we've learned that we really are concerned about patients that are high risk prostate cancer versus those that are low risk.

For example on my practice at Duke, my active surveillance numbers were about 17%. Up here in Syracuse my active surveillance rates are close to 40 to 45%. So a number of these patients that get diagnosed have low grade disease or are low risk patients and indeed many of those patients can be followed and identified by primary care physicians.

Typically, the identification of prostate cancer is done using a digital rectal examination and a PSA reading. And over the years our practices evolved a little bit and we'll talk about PSA testing in just a moment.

But I believe that the Exo test is a terrific test. It's been utilized in my practice for a number of years and really the goal is to try to identify patients that have high risk - that are high risk for high grade disease.

Those are the patients that I really want to treat. Those are the ones that urologists will make the most impact on and the low risk patients to identify those patients if we have a test that can be utilized in the primary care setting, the Exo test seems to be a very good test to try to identify patients that are either low risk or high risk and if they're high risk, then they can be referred to a urologist to try to take care of them. So I think urologists can make the largest impact to treat high risk patients.

Next slide. If we look back at data from (David Crawford), PSA testing, at least in the primary care markets, is almost 90% of all the PSAs that are done. Urologists make up about 7% or 8% of PSA testing, oncologists 3% to 4%, but clearly the primary PSA testing is being done by primary care physicians.

And a lot of primary care physicians don't, you know, understand PSA testing completely and I think that if we have test that really is trying to identify the high risk versus the low risk patients, that test will be a significant test to our armamentarium to try to identify patients, you know, that have either high risk or low risk because many of those low risk patients do not need to be treated and are best, you know, followed with an active surveillance protocol.

I think we know that early detection saves lives and patients that are identified especially if they have high risk, that landscape has really changed over the years on how we identify these patients. If - the nice thing about this test is many primary care physicians are not doing digital rectal examinations any more.

So at least in our practice that we've seen, you know, the primary care physicians may order a PSA test, don't do digital rectal examinations and they don't really know

how to react to those PSA readings even though they're doing the majority of the testing.

So what ends up happening at least in my practice, I monitor these patients for years that may have low risk prostate cancer that could be followed by, you know, other physicians, other than, you know, urologists.

So if we look at the specificity of PSA testing, it's only - it ranges between 51% and 68% for high grade prostate cancer. If we look at the ExoDx test, that sensitivity reading is close to 92%. So here we have a superior test, at least to try to identity high grade prostate cancer.

Next slide. I worked very closely with my primary care physicians in this community. We've educated them. They are - they have a significant role in taking care of patients and, you know, having a test that's available, if we can go to the next slide, you know, the ExoDx is simple to interpret. It's not complicated like different genetic testing that's out there. It's a very simple test to do.

During COVID, you know, many of these patients did not want to come in to the office. There is a home kit that's available so patients can actually - we can do televisits for these patients, have them receive a home kit. They urinate into a cup. We get the analysis back relatively quickly and we can address whether these patients have high grade or low grade cancer.

So I think that this test makes for more efficiencies in a practice. In our practice we utilize this test, PSA testing. And I believe that, you know, in our community, the primary care physicians are sophisticated enough to understand this test.

They've used it and I think it does boost the differentiation between high grade and low grade prostate cancer identification for individuals.

I would recommend that we allow this to be used by primary care physicians. The workload for urologists is quite high. There is, you know, fewer and fewer urologists graduating from residency programs. There's a high turnover of retirement of physicians in practice.

And if we can work with our physician partners, your primary care physicians, to try to identify patients with low risk prostate cancer, that will free up more space in time for the urologist to have the availability to see these high risk prostate cancer patients.

In my practice, these are the patients that I want to focus on, the high risk prostate cancer. The low risk prostate cancer patient can be followed and again, you know, as I said, you know, PSA testing is being done primarily by the primary care physician.

This is just one more test that allows the primary care physician to make referrals to the urologist when it's extremely important and necessary. So next slide.

So in summary we use this test, our physician partners and primary care medicine in the Syracuse area have used this test. They found the test to be useful. It's relatively straight-forward to explain to the patient. It's an easy test for patients to obtain.

We can continue with - we've seen different outbreaks of COVID and patients are reluctant to come in to the office. It's a great test to use in our armamentarium and when we can't even see patients in the office we can do televisits and we can do this

test and have good understanding if patients have low risk prostate cancer or high risk prostate cancer.

I'd be happy to answer any questions people might have on what we do with our practice here.

Dr. Awodele: So are you done, doctor?

Dr. Albala: Yes, yes.

Dr. Awodele: Okay. Yes, so thank you very much for your presentation. And if you could just please - follow up with comments as Dr. Noel said after the previous presentation we would appreciate that.

Dr. Cooperberg is on the call I understand. We did not get any slide from you, Dr. Cooperberg. Are you...

Dr. Cooperberg: Yes, I'll just make some comments, if that's okay. I'm actually on my way to the airport so I'm audio only. But I can make comments just verbally if that's all right with you.

Dr. Awodele: Okay, go ahead.

Dr. Cooperberg: Great. So I am a urologist-oncologist at University of California San Francisco where I co-lead the Prostate Cancer program. I'm also Service Chief at San Francisco VA. I've been doing Prostate Cancer research for almost 20 years, about 400 publications on the topic, including a lot of work on the area of screening and optimizing screening.

And, you know, where we are now with prostate cancer screening and the use of PSA ancillary tests, we think it's really finally after many, many years of pendulum shifts in both directions, getting us closer to where we need to be for a concept of smarter screening and treatment.

As I'm sure everyone is well aware, when PSA first hit the market in 1990s there were huge rates of over detection and subsequent over treatment of low risk prostate cancer in the course of trying to find the aggressive prostate cancers and over years as we increasingly understood low risk prostate cancer is almost never lethal and almost never causes any clinical symptoms.

We, in the academic world, and finally in community practice in the last, you know, in the current decade and the last decade have really begun to adopt the notion of active surveillance for low risk prostate cancer. Surveillance entailing serial PSAs and repeat imaging test and MRI.

However, active surveillance is still relatively intensive protocol for many men. It does require life-long surveillance. It does - really does require the MRIs and the biopsies which are quite expensive which do pose low but real risk of sepsis, et cetera, and which ultimately can lead to over treatment even down the road given the vagaries of pathology interpretation, et cetera.

So we're increasingly coming to understand that the best way to manage low risk prostate cancer is not to find it in the first place. And we have really been focusing more attention in recent years on the notion of over diagnoses as the prelude to over treatment.

Now the 2012 US preventative services task force recommendation that no men should undergo PSA testing ever was a direct reaction to the problems of over diagnosis and over treatment which we witnessed through the 1990s, early 2000s.

The current recommendation per shared- decision making is basically held across all the various guidelines. But there is still relatively little guidance in terms of what to do with the PSAs and what thresholds we should use, et cetera.

And what we're really coming to realize with some excellent, excellent research that's been done in different countries, in different settings with different racial groups, et cetera, in the last 10 years is that PSA is an incredibly good test. It's probably the best biomarker in the history of oncology if it's used well which means, using it, focusing efforts for screening among younger men and using a low threshold to determine secondary testing.

About 75% of the population who gets a PSA test has value under one and can basically stop worrying about prostate cancer for the next 20 years. But we have no interest in biopsying everybody with marginal PSAs and that's where biomarkers have really become an absolutely integral part of armamentarium.

At UCSF and many other practice, academic and community practices we've been using urine and serum tests for a number of years now as well as MRI to help determine who actually need the biopsy. Because like Dr. Albala said, you know, we really want to focus our efforts on high risk prostate cancers and avoid treating low risk prostate cancers or better still, to not find the low risk ones because we're increasingly confident that the low risk cancers almost never progress to a clinically meaningful state.

So we are using tests like EPI pretty heavily. As Dr. Albala mentioned, the fact that the company released its home kit shortly after the onset of the COVID pandemic, was incredibly fortuitous, because it meant we can keep patients out of the office, avoid having them come in to do the DRE, which was required for other urine tests and not even have to come in to a lab to get a blood draw.

So in the telehealth era which for us is persistent. We are still 70% telehealth and probably will be forever. There's a very big advantage; patients love it. They love not driving, and paying for parking. So we're using tests like this and we are using EPI specifically and quite heavily because of the favorable logistics.

But at the end of the day it's still not a particularly efficient use of time and specialty resources to have all these men in urology practice when so many of them to basically be ruled out for clinically significant prostate cancer at arm's length with a test like EPI.

So we've been working very, very closely with our primary care leadership at UCSF and across UCSF Health now, across our network for the last several years to try to take on this problem.

UCSF primary care and to really emphasize the point Dr. Albala already made, it is primary care not urology that does the vast majority of prostate cancer screenings and PSA ordering.

So, you know, UCSF primary care like many academic primary care departments throughout the last decade, were really in lock step with the task force and kind of believe prostate cancer screening didn't make much sense but we should do it.

And, you know, with the 2018 recommendation along with an increasing awareness of racial disparities and, you know, the better data coming out in support of screening, we have really reached a very strong consensus between primary care and urology, epidemiology and primary - and the primary general medicine

departments at UCSF in support of shared decision making for early detection which is now baked into our EMR system but with the explicit understanding that we have no interest in biopsying everybody with a slightly elevated PSA.

And, you know, we are using again just like EPI as well as MRI quite heavily, but, you know, for the primary care providers, they're very interested in the concept of using reflex testing at the point of care in primary care and, you know, this is the main point that I really want to speak to as far as this LCD is the restriction of the test to urology and oncology. Because at the end of the day by far the most efficient pathway, an efficient use of limited time and dollar resources for patients with a slightly elevated PSA is to have a savvy primary care provider, send off a home kit, get the EPI score back and if it's below threshold, we're pretty much done.

The patient can go back to periodic PSA surveillance or if PSA is low, you know, infrequent PSA surveillance and have really started to make these quite formal in terms of protocols across the uses of health enterprise.

I would say it is still a minority of primary care practices and clinics that have adopted this whole-heartedly, but it's a concept which resonates very strongly with the primary care community and it works well. We've talked about this with the number of the different blood and urine tests that are out there, it works particularly well for EPI again because of the home kit availability and because the test does have a clear threshold on it, associated with a very good negative predictive value which at the end of the day is what we want to know for men with a marginally elevated PSA contemplating skipping the biopsy.

So, you know, I really would - the main - that and the points that DRE in this day and age actually offers very little for men when we are driving referrals based on low PSA thresholds. The older literature is certainly full of occasional examples of high risk cancers found with low PSAs and positive DREs.

But the fact that the DRE really becomes part of work-up not screening and the value of DRE in primary care is quite limited.

So, you know, our path forward and I hope this will be supported by coverage decisions really should be early baseline testing with low PSA to threshold for referral, liberal and heavy use of secondary markers like EPI as reflex tests which can be done in a primary care community combined with MR to drive by the decision making so that ultimately we only biopsy men in whom we expect we might find the higher risk cancers that actually gets to be treated.

Dr. Awodele: Okay, thank you very much, Dr. Cooperberg. And as we said on this call, please send in your comments in writing to partblcdcomments@anthem.com and this email can be found, you know, on the draft LCD that you just commented on. So thank you very much for your comments. And so, operator, if you could please. Oh thank you. if you could see it's open up the line for comments from the public please. Thank you.

Coordinator: Absolutely. If you have any comments at this time, please press star 1 on your phone. Be sure your line is unmuted and record your name so you may be introduced.

Again that's star 1 for any comments. One moment as I wait for them to come through. And we have a comment from Dr. Eric Loo. Go ahead, please, your line is open.

Dr. Eric Loo: Hello can you hear me okay?

Dr. Awodele: Yes, we can.

Dr. Eric Loo: Okay. I'm not an expert in PSA testing and urology and that type of stuff. I'm a pathologist. I focus in molecular genetics and hematopathology so like leukemia and lymphomas. But I just wanted to add a quick comment on to our last speaker from UCSF.

I do recall back when I was in training, you know, 10 years ago, you know, my mentors who were focused in, you know, prostate pathology pretty much had the very similar things to say as the last speaker.

So I just wanted to echo in that, you know, what he was saying sounds correct also from the pathology standpoint and hopefully, you know, this is – going to be helpful for a lot of men with - to prevent them from getting over treatment.

Dr. Awodele: Thank you, doctor. Thank you. It's nice to hear from various aspects of this so we do appreciate your comment. Any other people with comments on the line?

Coordinator: I'm showing no further comments at this time.

Dr. Awodele: Okay, thank you. So the official comment period for the draft LCD that we presented on this call, at this open meeting ends on July 23, 2022. The comment period for people who are not aware, it's a period of time from when the LCD, the draft first became forward facing or open to the public which was on the ninth of June 2022 and it's a forty-five-day period which ends July 23, 2022. Next slide please.

And just as a reminder, to comment on any of the proposed LCD that we presented during their official period, please send your comments through PartBLCDComments@anthem.com. And if your choice is snail mail, national government services, Inc., LCD comments PO Box 7108 Indianapolis, Indiana, 46207-7108.

And with that, this public meeting is officially closed and I would like to wish everybody a safe and fun 4th of July weekend. Thank you very much. Operator, you can disconnect.

Coordinator: Thank you. That would conclude today's conference and we thank you for participating. You may disconnect at this time. Having a wonderful day.

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