National Government Services INC

Moderator: Dr. Gina Mullen
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1:00 p.m. CT

Coordinator: Welcome and thank you for standing by. For the duration of today's conference, all participants will be in a listen-only mode. I'd like to inform all parties that today's conference is being recorded. If you have any objections, you may disconnect at this time. I would now like to turn the conference over to Dr. Mullen. Thank you. You may begin.

Gina Mullen: Good afternoon everyone, and welcome to the Contractor Advisory Committee, or CAC Meeting on KidneyIntelX test. My name is Gina Mullen and I'm a Contract Medical Director with NGS.

The purpose of today's session is outlined in CMS IOM Publication 100-08, Chapter 13, Section 13.2.4.3. And I'll give some of the highlights of our process in a little bit. Basically, the purpose of today's meeting is to listen to our distinguished subject matter experts evaluate the medical evidence regarding KidneyIntelX test.

Please understand that this meeting is open to the public. However, only the contractor medical directors and the subject matter experts will be permitted to speak. As a point of clarification, please understand that the company, Renalytix, will have two identical tests on the market starting in 2024, one called KidneyIntelX and one called KidneyIntelX.dkd.

The FDA has approved the KidneyIntelX.dkd and given the test a suffix designated as .dkd for name distinction. As you are aware, FDA approval does not constitute Medicare approval for medically necessary testing. In order to avoid confusion during the CAC, we will address the two identical tests.

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We will also include the following statement and the questions regarding KidneyIntelX, which will indicate that the test is an AI-enabled prognostic testing platform to guide care management for adults with type 2 diabetes and chronic diabetic kidney disease.

Before we go any further, I ask our panel of five experts to please introduce yourselves. Please state your name, affiliation, and acknowledge any possible conflicts of interest. Let's start with Dr. Gondal.

Maryam Gondal: Hi, my name is Maryam Gondal. I am a Nephrologist with Yale University. I do not have anything to declare. There is no conflict of interest.

Gina Mullen: Thank you. Dr. Rimmer?

Jeffrey Rimmer: I'm Jeffrey Rimmer. I'm a Nephrologist. I am a Professor Emeritus at the Larner College of Medicine, the University of Vermont. I currently still am the Medical Director of the University of Vermont Medical Center Dialysis System, and I'm the Director of the CKD Navigator Program at the University of Vermont Health Network.

Gina Mullen: Thank you, Dr. Rimmer. Dr. Ross?

Mike Ross: Yes, Hi. My name is Mike Ross. I'm the Chief of Nephrology at the Albert Einstein College of Medicine in the Montefiore Medical Center. I have looked into implementing the KidneyIntelX at my own institution at some point, but I have no financial stake in any way and have never received any money from the company. So I don't have any conflict.

Gina Mullen: Thank you. Dr. Jacobs?

Charles Jacobs: Hello. I'm Dr. Charles Jacobs. I'm a Nephrologist at Maine General Medical Center in Waterville and Augusta, Maine. And I don't have any conflicts of interest either.

Gina Mullen: Thank you, Dr. Jacobs. Dr. Kimball? Dr. Kimball?

Catherine Kimball: Yes?

Gina Mullen: Oh, sorry we couldn't hear you.

Catherine Kimball: Oh, okay. I'm Catherine Kimball. I'm a family practice doctor in Waterville, Maine; part of Northern Light system in the state of Maine. I have no conflicts to declare.

Gina Mullen: Thank you so much. Next on the agenda are key questions and discussion. Prior to this meeting, NGS completed a review of the literature and prepared a list of articles for review by our subject matter experts. Our panel of experts will comment on these articles and any additional evidence of which they may be aware.

We have prepared and will read a series of 12 questions, ask the subject matter experts for his or her response, and then ask the other subject matter experts if they have anything to add. We have roughly five minutes for each question. The answers to these questions should be based on the literature and be in alignment with good clinical practice. Please vote your confidence level from 1 to 5, 1 being low confidence and 5 representing high confidence. Also, if the literature is silent or inconclusive on a particular issue, we would appreciate our subject matter experts noting that.

We will now begin with the questions. Dr. Gondal, if you would be so kind to start us off. Question Number one, how confident are you that there is adequate published evidence that the use of KidneyIntelX tests, which is an AI-enabled prognostic testing platform, improves health outcomes in patients with type 2 diabetes and early stage chronic kidney disease stages 1 through 3b?

Maryam Gondal: So, based on the literature that I have read and reviewed, I am sufficiently confident that this test will add to the current measures that we are actually using for diabetic kidney disease. This is, as we all know, an AI-generated prognostic test which keeps in view certain biomarkers which have already been proven that they do talk about.

They do tell us about TNF1, TNF2, and KIM. They do talk – tell us about the progression of disease, kidney disease. So this is based on the literature is a reasonable test to incorporate into our practice.

Gina Mullen: Thank you. Does anyone have anything to add?

Charles Jacobs: Can I – this is Dr. Jacobs calling.

Gina Mullen: Yes, please, Dr. Jacobs.

Charles Jacobs: Can I add maybe – I don't know if everybody here is a little confused about these two tests or not. And I did actually reach out to the Renalytix Company and try to get a little clarification. And I think I have some on that. Is that something that people might want to know now or should we wait 'til the end of the meeting or my presentation?

Gina Mullen: Feel free to share if you have any comments to the question. Yes, sir.

Charles Jacobs: So from what I can tell, you know, the reason that there are these two tests and I actually got a response from Dr. Coca, who was one of the people who worked there, is that this has to do with the difference between the CKD-EPI equation from 2009 versus the CKD-EPI equation from 2021.

And I believe that the test with the .dkd will be used for patients who present - who give GFRs with the CKD-EPI 2021 calculation and the other test will be used for the CKD 2009 equation. And he noted that they have validated their data for both equations. I hope that…

Mike Ross: That's helpful.

Charles Jacobs: Yes. I don't know if anybody else was confused about any of that in their literature, et cetera.

Gina Mullen: Thank you so much.

Mike Ross: And it's reasonable that they would need separate algorithms considering the equation, different and will give different results. So that makes sense.

Charles Jacobs: Yes, I think they - you know, from what – I think the results probably are the same with both equations, with the algorithm. It was sort of what he implied, but I think they kind of have to call them two different tests because, you know, just sort of the way the literature, - you know, they just were unfortunate to sort of present all of their literature in 2021.

But their data really is mostly with patients who were in - you know, prior to who would have had a CKD earlier, CKD 1. I'm not going to take up any more time with that. Thank you so much.

Gina Mullen: No, I appreciate that. The next question is for Dr. Gondal. Question Number two, how confident are…

((Crosstalk))

Mike Ross: Can I just make one other comment on that first? So...

Gina Mullen: Yes, of course, yes.

Mike Ross: We have to be a little careful with showing that it improves health outcomes. I mean, all the studies, while I do believe this is likely going to be a valuable test, these are all association studies for the most part. So, we don't – you know, they haven't shown per se that this test will directly improve outcomes. I have hoped that it will, but, you know, I think that remains to be proven.

Jeffrey Rimmer: So, this is Dr. Rimmer. I would like to concur with that statement as well in terms of answering the specific question which asks about the impact improving health outcomes. And while it is a very promising, interesting test, there's minimal to no evidence with regard to actually demonstrating improved health outcomes.

Gina Mullen: Thank you all for that discussion. I'm going to go to the next question. Question Number 2 for Dr. Gondal. How confident are you that there is adequate published evidence that KidneyIntelX test, which is an AI-enabled prognostic testing platform, accurately predicts the risk of early stage kidney disease progression?

Maryam Gondal: Can you guys hear me?

Gina Mullen: Yes, I can hear you now.

Maryam Gondal: Okay. Okay. Sorry. I guess what I said was kind of just – couldn't hear anyone. So based on the evidence that I have seen, it is a test which basically is going to divide patients into low, intermediate, and high risk. Again, you know, it all boils down to this is a test that cannot be used alone. It has to be used in – along with the other parameters that we currently are using for diabetic kidney disease and for CKD.

So as an adjunct to what we are already doing, this test will be helpful. Again, this test cannot be used as the sole reason to predict the risk of progression in early CKD. But with all the other tests that we do, this can add value to the current management that we have and can actually help and further assess referrals that need to be made by the primary care physicians or for adding more - you know, just to see what the progression is going to be in patients. So it can be used as an adjunct but cannot, I'll just clarify, cannot be used alone.

Gina Mullen: Thank you. Does anyone have anything to add? All right. One more for Dr. Gondal. Question Number 3, if at least intermediate confidence greater than or equal to three is noted in questions 1 or 2, how confident are you that there is sufficient published evidence to recommend guidelines for proper use of KidneyIntelX test, an AI-enabled prognostic testing platform in the care management of Medicare patients with type 2 diabetes and chronic diabetic kidney disease.

Maryam Gondal: So, I guess all these, you know, questions are, of course, interrelated and the evidence, of course, is not going to be extremely robust. But this test was also used as a post-hoc analysis

in the canvas trial and is being, you know, carried out in another research that was initially done in Monte.

So I actually at this time do feel if we add on this test to all the current measures that we have, it will be of value for managing patients with type 2 diabetes and chronic kidney disease.

Gina Mullen: Okay. Thank you. Does anyone have anything to add to that?

Catherine Kimball: Dr. Kimball here. I would just make the note that its value is somewhat dependent on getting all those other values out of the EHR. So, either the tests need to be done or they need to be accessible. And I don't know if that limits its utilization in either certain populations or not.

Mike Ross: This is Mike Ross. At least in my own experience looking into – getting into my institution, it is - it certainly makes it cumbersome because they need to be able to abstract a limited number of clinical variables. I think like six or seven clinical variables that they need to get from the medical record.

So that makes it more cumbersome and less able to be just rolled out everywhere around the world. But I do think it still – I don't think it limits the usefulness of it when it is implemented. I think, you know, there are some sort of unique – it's able to generate unique information because of all the different types of data that it combines, but it does make it more difficult and costly.

((Crosstalk))

Gina Mullen: We're going to focus on the literature not so much cost and implementation.

Mike Ross: Okay.

Gina Mullen: Thank you so much. Well, let's move on to Dr. Rimmer. Question Number 4. How confident are you that there is adequate published evidence that KidneyIntelX test, which is an AI-enabled prognostic testing platform, is an integral component to aid in the medical management of CKD and Medicare beneficiary?

Jeffrey Rimmer: All right. Slightly long answer. The test was trained and tested on samples derived from two populations in the mid-Atlantic region of the United States. Subjects who met the criteria for early diabetic kidney disease were selected from the biobanks maintained by the Icahn School of Medicine at Mount Sinai and the University of Pennsylvania Health system.

There were a total of 1146 subjects who were identified. There was a reasonable mix of ethnicities. The median age for the population was 63 years, with an upper boundary of the third quartile being 69 years. Presumably, 30% to 40% of the study population would have been age eligible for Medicare.

There is no reported interaction between age and the predictive ability of the test. The vendor web site states the only age restriction is that subject should be 21 years of age. The derivation population was geographically limited, suggesting that regional influences on the risk of progression of kidney disease could be missed by the test.

The canvas study population was geographically diverse, both young and ethnically homogeneous. Application of the original algorithm to the canvas population with early diabetic kidney disease without additional training or testing produced results similar to the derivation study. This supports the probability that regional differences are unlikely to affect the test results. The test is likely applicable to the Medicare population.

Questioning the value of the test as a component of management and this relates to the prior question implies that a system exists in which the test is embedded in health care settings, where there is a systematic approach to persons with diabetic kidney disease. The KidneyIntelX test may well be an important component in decision making. Currently, there is little or no prospective evidence of improved medical outcomes with its use. That's it.

Gina Mullen: Thank you, Dr. Rimmer. Does anyone have anything to add? All right. The next question is for Dr. Rimmer. Question Number 5. How confident are you that this KidneyIntelX test, which is an AI-enabled prognostic testing platform, offers more clinical importance than albuminuria and EGFR to clinicians in making treatment decisions?

Jeffrey Rimmer: So, this is a short one. The predictive ability of the KidneyIntelX test was compared with that of the KDIGO risk stratification based on EGFR and urine albumin creatinine ratio measurements in both the derivation and validation study and when the machine learning model was applied to patients with early diabetic kidney disease who participated in the canvas study.

In both cases, the KidneyIntelX predictions were superior. The KidneyIntelX test likely offers more utility for decision making to clinicians than KDIGO risk stratification based on static measurements of EGFR and urine albumin creatinine ratio. Done.

Gina Mullen: Thank you so much, Dr. Rimmer. Does anyone else have any comments? Moving on to Dr. Ross. Question Number 6. How confident are you that based on the clinical utility of KidneyIntelX on patients with early stage diabetic kidney disease, a real world evidence study, KidneyIntelX test has resulted in changes in clinical management by clinicians?

Mike Ross: So, in this study, they looked at about 1600+ patients at Mount Sinai with CKD stages 3A and B and Stage 1 and 2 with albuminuria over a two-year period. And they looked at – they collected data six months before the test, which served as the baseline. And then they measured – they did the measurement and then they looked at the six months after the test to see basically what the clinicians did with the information.

And, you know, the most important things that they found was there was a 20% increase in referrals to specialty services like dietitians or endocrinologists or nephrologists. And there was also a significant increase in the use of medications that are important to managing these patients like ACE inhibitors and (COX-2) inhibitors and other important medications.

And, you know, which is, you know, potentially very important because what – everybody knows that in late stage CKD you need to be aggressive. But most of the patients with early stage, you know, Stage 1, 2, especially early 3, especially if they don't have really severe albuminuria, most people just never even think twice about these patients.

So, the main value I do think they showed is that this is kind of a red flag regarding patients that often don't have any further testing or referrals that something needs to be done. So, I do think even though this was not a randomized trial or anything like that, I do think it was highly suggestive that it does serve as a way to increase the medical care that should be given to these patients anyway, but usually is not.

But it did not show any effect on health outcomes, you know, like, you know, kidney failure or anything like that. It was really just showing that clinicians tend to act on this information when they have it.

Gina Mullen: Thank you, Dr. Ross. Does anyone have anything to add? The next question is for Dr. Ross. Question Number 7. How confident are you that there is adequate published evidence that KidneyIntelX, which is an AI-enabled prognostic testing platform, will improve prediction of near term kidney disease progression and outcomes in patients with type 2 diabetes and diabetic kidney disease?

Mike Ross: Okay. So, one problem I have with this question is I don't really know what near term means, but since this test will not – you know, a test doesn't directly impact kidney disease. It's what clinicians do with the test. So the interventions that we have for diabetic kidney disease, like COX-2 inhibitors and ACE inhibitors take about two or more years to have their beneficial effects.

So if near term means in, you know, two or three years, then I do think it's likely that this test can have an effect in the near term, like I said, two plus years, because I do think it will lead to more patients being treated with medications and nonmedication strategies that will reduce progression in that timeframe.

Gina Mullen: Okay. Thank you so much. Does anyone have anything to add? And the next question for you, Dr. Ross. Question Number eight. How confident are you that further randomized controlled trials are not necessary to evaluate the efficacy of KidneyIntelX, which is an AI-enabled prognostic testing platform, and to identify reduced KidneyIntelX risk scores as a result of initial management?

Mike Ross: So, this is another hard question for me because as, you know, an investigator, I always want randomized controlled trials whenever we can get them. And I do think it will be important down the road to have randomized controlled trials to see what the effect of this is on (heart) outcomes, especially – because I don't think our current evidence would support this being the standard of care that everybody needs to do.

I think the current evidence supports that this is a very likely, very useful test that will be up to individual medical centers and clinicians whether they, you know, want to implement. So, I think the main reason we need randomized controlled trials is to really nail down the effect on outcomes, which would then really make this a test that really need it really needs to be done as part of guidelines. Right now, I don't think guidelines can say that we need to do this.

Gina Mullen: Thank you. Does anyone else have any comments? Thank you, Dr. Ross. Moving on to Dr. Jacobs. Question Number 9. How confident are you that there is adequate published evidence that KidneyIntelX, which is an AI-enabled prognostic testing platform, helps decrease socioeconomic disparities in patient groups due to lack of accurate tools to assess those at greatest risk for CKD progression?

Charles Jacobs: Hello, this is Dr. Jacobs. You know, as Dr. Rimmer described, the KidneyIntelX algorithm was developed in a socioeconomically diverse set of patients; 7.1% of the patients were white, 39.7% of the patients had African ancestry, and 47.3% of the patients were identified as Hispanic/Latino.

And this ethnic demonstration would usually include nearly all groups at high risk for CKD progression and adverse outcomes. People with Native American heritage may be missing from that group would be the only thing that I would note.

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So overall, I do think it would include the groups that are at highest risk to have adverse outcomes. And I also did discuss earlier the bit about the difference between the CKD 2009 and CKD 2021 equation. And there is a - that's part of the recent publications that were presented at the diabetes meeting. And in my written notes I'll have a reference to that. Thank you very much.

Gina Mullen: Thank you, Dr. Jacobs. Does anyone have anything to add? Next question for Dr. – oh, sorry. Was there somebody who needs to speak? Next question for Dr. Jacobs. Question Number 10. How confident are you that there is adequately published evidence that the KidneyIntelX test, which is an AI-enabled prognostic testing platform, is generalizable to the Medicare patient population?

Charles Jacobs: I hope I don't go too far out into left field on this. But, you know, this test is marketed towards primary care providers as a package that includes education and clinical guidelines. In order to give the most accurate results, the patient's records need to be in an integrated electronic medical record system where all the other clinical data are available for query.

In order to optimize outcomes in the high-risk patients, availability of specialty care is also required. For example, Renalytix latex has marketed this to the Veterans Administration, and that's a good target with an integrated EMR and access to some specialty care.

And there certainly exists a large Medicare population that could also meet this criteria. I would say that it's concentrated in urban centers that also have tertiary medical care centers. From a geographic standpoint, many rural Medicare members would not have their records in a single EMR, and their primary care providers would not have easy access to advanced specialty care for diabetes or renal disease.

So my confidence level is certainly in the – would be – I'd give this answer a three right in the middle of the confidence level that it could be generalizable to the Medicare patient population.

Gina Mullen: All right. Thank you, Dr. Jacobs. Does anyone else have any comments? Moving on to Dr. Kimball. Question Number 11. How confident are you that the evidence regarding the use of the KidneyIntelX test, which is an AI-enabled prognostic testing platform, changes clinical best practice and management of the Medicare patient population with type 2 diabetes and diabetic kidney disease for CKD progression.

Catherine Kimball: I think that the literature provided does support the idea that this test changes best practice and management by identifying patients at risk for further progression into more serious CKD earlier and gives us in primary care as well as specialty – specialists that we might refer to an opportunity to intervene earlier and perhaps preserve kidney function for longer.

And I felt that the literature that we were offered to review supported that. I agree with what has been spoken of earlier with regard to seeing more studies that demonstrate more outcomes, more broad outcomes than just – that we referred earlier – that the providers referred earlier to specialists and changed their approach to those patients. I'd be curious to see more outcomes trials to show that it had an impact on how many patients end up on dialysis or needing kidney transplant, et cetera.

Gina Mullen: Thank you. Does anyone have anything to add? Question Number 12. How confident are you that the evidence regarding the use of the KidneyIntelX test, which is an AI-enabled prognostic testing platform, improves clinical decision making and clinical outcomes of the Medicare patient population with type 2 diabetes and diabetic kidney disease for CKD progression.

Catherine Kimball: I was I think that the - that it does improve clinical decision making by identifying patients earlier as well as into medium and high-risk categories. And it may also – I wasn't clear whether or not it would possibly improve the testing for these patients by needing the data from the EMR as well, which helps inform us. But I think this put it into a format that makes it easier for clinicians to act on the changes that are seen by this test.

Gina Mullen: Thank you. Does anyone have anything to add? Okay, now to our closing remarks. I do want to thank the subject matter experts who participated today. In addition to your expertise, it does take a certain amount of courage and commitment to provide this kind of input publicly in a public forum like this.

We appreciate it and will be taking the information that you've given us into consideration as we consider our next steps moving forward. Any further comments from our speakers or medical directors? Since there are no further comments being offered today, the meeting is now closed.

END